THE DIGITAL CIRCULATION

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To MURIEL
JUDITH
SUSAN
and BENJAMIN

PREFACE

A BOOK on a subject apparently so limited as the digital circulation needs some justification. Investigation of this subject is of importance for three principal reasons: first, when properly studied the digital circulation may mirror changes that take place in the systemic circulation as a whole; second, changes in the peripheral blood vessels, whether structural or functional, are very often manifest to the greatest degree in the acral parts of the circulation, namely the fingers and toes; and third, the circulation in the fingers and toes may be studied easily with comparatively simple, bloodless methods entailing little discomfort to the patient.

Since the acral circulation is subject to such extreme fluctuation with temperature change, pain or emotion, whereas the systemic circulation represents the resultant of events that take place in the various vascular beds which it supplies with blood, it may be difficult to understand how the digital circulation can be considered to reflect changes in the systemic circulation as a whole. The digital circulation may, however, be stabilized by inhibiting sympathetic nerve discharge and may then accurately reflect non-neurogenic or intrinsic changes in the entire systemic circulation, as, for example, in hypertension.[39]

The second reason for studying the digital circulation is the fact that structural and functional changes are often most manifest in the acral portions of the circulation. The effects of cold, for example, are frequently most pronounced in the fingers and toes.[illegible] Emotions affect the circulation in the fingers and toes to a greater extent than any other part of the systemic circulation. The same may be said of such general circulatory disturbances as shock, in which the most pronounced and earliest changes are also in the periphery.[1]

The third factor is the ease and convenience with which the peripheral circulation may be studied. All the available methods, skin temperature measurement,[illegible] plethysmographic,[73] photoelectric[illegible] or calorimetric[illegible] techniques, are bloodless methods applicable at the bedside. Other methods for studying blood flow, including the measurement of cardiac output[225]

are usually cumbersome and time consuming and often not bloodless The patient may not therefore, achieve the so called basal state without diffi culty Even the arm [64] foot [550] or leg[1] plethysmographs are cumbersome instruments requiring exacting technics *which are beset with numerous* pitfalls It should be pointed out however that various methods for measuring blood flow have their specific uses, and that these technics *may in many instances supplement one another*

Sufficient information about the digital circulation has been accumulated to warrant its presentation at the present time in monograph form Some of this information is available from the published work of others the remainder having been collected by the author It is the purpose of this book hence to present all the available data on the digital circulation in a coherent, organized manner pointing out the gaps in our knowledge in the hope that these may be narrowed by future investigation

The historical background for the study of the digital circulation has been provided by the development of medicine and its branches over the course of many years It was Hippocrates, [65] for example who first de scribed clubbed fingers and the discovery of the circulation of the blood by Cesalpino[100] and by Harvey [46] made possible the development of many phases of physiology and medicine including the study of the digital circulation More recently the anatomic investigations of Hoyer [278] Sucquet [561a] and Grant and his co workers[193 0] have established the im portance of arteriovenous communications in the digits and Barre[36] has described the clinical and Masson and Gery [376] the pathologic features of glomangiomata

Study of the digital circulation as such however began with the development of methods for its investigation In Austria in 1899 Gaert ner[150] described a capsule for measuring systolic blood pressure in the finger This method originally devised to measure systemic blood pressure as a whole was ultimately supplanted by the Riva Rocci [457] Korotkow [305] method Digital diastolic arterial pressure was first measured by the author in 1938[389] employing a principle established for the arm by von Recklinghausen [59] Several workers since then have introduced modifica tions and improvements in the measurement of digital blood pressure [337 596]

Nail fold capillaroscopy was first described by Lombard[361] in the United States and developed in Germany in the early part of the twentieth century by Weiss and Muller[597] among others The subject was compre hensively reviewed by Wright and Duryee[630] and subsequently by Roth [493] The capillaroscope made possible the direct and accurate measurement of capillary blood pressure by Carrier [97] Landis [3 6] Eichna[143] and their co workers The phlebomanometer developed by Burch and Winsor [ ] made it possible in addition to measure venous pressure in small veins

Study of skin temperature was greatly stimulated by the appearance of electric thermometry at first with thermocouples and later with other

devices [43, 426, 417] The English group under the direction of Lewis Pickering and Grant[35, 255] made great strides in understanding the digital circulation through the use of these instruments In this country the Mayo Clinic group including Brown [9] Adson [70] Allen [17] Barker [11] Hines [17] Roth and many others contributed to our knowledge of the digital circulation by studying skin temperatures In Boston White and Smithwick [601] Freeman [159] who continued his work in California and Gibbon and Landis[151] all made use of the thermocouple as a recording device for studying circulatory changes in digits More recently Burton[90] has reviewed the entire subject

Study of the pulsation of small vessels in the digits was meanwhile developed by several groups of workers throughout the world Goetz introduced the digital plethysmograph in 1935 in Germany [155] Burton[91] in Canada Turner Burch and Sodeman[575, 59] in New Orleans and Wilkins Doupe and Newman [611] then working in England devised similar instruments The plethysmograph was subsequently made portable by Burch [77, 5] The photoelectric plethysmograph was already in use in 1938[419] when Hertzman [2] began extensive studies with this instrument in St Louis Photoelectric devices for the study of digital pulsations have also been used in Germany [227] and in Denmark [4] All of these workers used the digital plethysmograph to measure blood flow after venous obstruction They adapted the venous obstruction technic established for the arm by Hewlett and van Zwaluwenberg [244] to the finger Oscillometry was first introduced in France by Pachon[450] in 1909 and was developed there chiefly for measuring the pulsation of large blood vessels Graphic oscillometry followed [179] and recently Johnson [9, 90, 9] Lax [337] and their co workers have adapted oscillometry to the study of digital pulsations

Advances in the clinical knowledge of this subject kept pace with those in methodology Raynaud s description of the condition which bears his name called attention to disorders of the digital circulation in 1862 [475, 490] Von Winiwarter [593] in Germany and Buerger [5] in this country described thromboangiitis obliterans Knowledge of arteriosclerosis and other peripheral vascular diseases was advanced through the investigations of many workers throughout the world [115, 330, 419, 488, 585] Although preceded by several investigators [119b, 340] White and Smithwick[601] in Boston and Adson [11] Brown [1] Allen [17] and their co workers in Rochester Minnesota used sympathectomy extensively and the effect of this operation on the peripheral circulation has gradually become clarified [11] The nature of Raynaud s disease was investigated by a host of workers including Hutchinson [96] Lewis [347, 345] Allen [18] Beyer and Wright [50] and many others

The author s part in the work embodied in this book began in 1938 in the laboratory of Sir Thomas Lewis His work there was made possible by the combined efforts of Drs Emmanuel Libman Louis Gross and Louis N

Katz The author s interest in clubbed fingers arose from a search for physiologic antitheses to shock after working with Gross and Katz on the effects of experimental coronary occlusion,[28–31, 410, 411] acute failure of the isolated heart,[49 491] and pulmonary embolism[388] Sir Thomas directed the author s attention away from consideration of cardiac output and other general facets of the circulation toward the peripheral circulation, *in the study of which his laboratory at that time excelled* The association between clubbed fingers and increased digital circulation was established and the Stewart hand calorimeter adapted to the digit[389-391, 407, 409]

From 1939 to 1952 except for the war years, the methods developed in London for the study of clubbing were applied to the study of other diseases at the Mount Sinai Hospital, and from 1951 to 1953 at the Columbia University Research Division of the Goldwater Memorial Hospital in New York[39, 395, 40, 405, 16, 414] Digital vascular resistance was also defined[395, 399] following principles established by Poiseuille[466] Whittaker and Winton,[600] Lamport[3, 3 5] Bingham[54 56] Boger and Wezler[61] Green[18] Pappenheimer[453] and many others In addition the effect on the hallucal circulation of sympathectomy for hypertension was clarified[414] Meanwhile other workers confirmed many of these results and extended research on the calorimeter These included Arnott and Macfie[3] Capriglione and Duque[96] Greenfield and his co workers[10, 18] and Wilson[6 1 6 a 6 b]

Studies by the author on the digital circulation were aided by grants from The Emmanuel Libman Fellowship Fund The Dazian Foundation The American Heart Association and The National Heart Institute These helped with the burden of many technical and secretarial details taken over by a succession of people including Misses M Spencer E Di Pasquale *J Shapiro P E Cohen A A Zanetti J Dayton S Haffka S Feigen*baum Mrs S Young Messrs R E Schwartz G Grossinger P E Ciri G Wiener H Rothman and S Roth Most of the photography was done by Mr R W Carlin Drs H A Abel G H Eurman E B Grossman S Alpert A Leslie and A W S Touroff have all cooperated directly in several phases of this work We are grateful to Drs S Feitelberg E B Grossman, A B Gutman I S Wright and D Seegal who have reviewed the manuscript critically *and to The Ciba Company which has generously* supported the cost of the color illustrations Many publishers journals and authors have been most cooperative in extending permission for the reproduction of illustrations and finally the publishers Grune & Stratton Inc have been very patient and helpful in the printing of this book

New York City MILTON MENDLOWITZ
January 1954

1

ANATOMY

The main arteries supplying the fingers and toes are the volar and plantar digital arteries respectively [10, 03, 463] These vessels are ultimate branches of the radial and ulnar arteries in the upper extremity and the posterior and anterior tibial and peroneal arteries in the lower [10, 203, 463] In the hand these digital arteries arise from the deep palmar arch via the interosseous arteries which also receive branches from the superficial palmar arch and perforating twigs from the dorsal arteries of the hand [10, 03, 463] The interosseous arteries divide into two volar digital arteries[2, 5] which run up the sides of the fingers and break up into smaller branches supplying the digital tissues [10, 03, 463] The inner volar artery of the thumb and the outer volar arteries of the forefinger and fifth finger arise directly from the deep and superficial arches The outer volar artery of the thumb arises directly from the radial artery [1, 3, 463] There are many possible variations and anomalies in the origin of these vessels from the palmar arches [615]

In the foot the lateral and medial plantar arteries arise from the posterior tibial [2, 463] These arteries also form an arch and give off interosseous branches which subsequently divide into digital plantar arteries supplying the tissues of the toes with blood [10, 203, 463] The outer plantar arteries of the great and fifth toe arise directly from the medial and lateral plantar arteries respectively [11, 03, 463] Branches of the medial plantar artery join the first second and third interosseous arteries [10, 203, 463] Here too many anomalies and variations in the origin of these vessels occur The *inter*osseous arteries also receive blood from perforating branches which arise from the dorsalis pedis artery a terminal of the anterior tibial artery [12, 3, 463] The peroneal artery anastomoses with the system and

Katz The author s interest in clubbed fingers arose from a search for physiologic antitheses to shock after working with Gross and Katz on the effects of experimental coronary occlusion [9–31 410 411] acute failure of the isolated heart, [49a 491] and pulmonary embolism [389] Sir Thomas directed the author s attention away from consideration of cardiac output and other general facets of the circulation toward the peripheral circulation in the study of which his laboratory at that time excelled The association between clubbed fingers and increased digital circulation was established and the Stewart hand calorimeter adapted to the digit [389-391 407 409]

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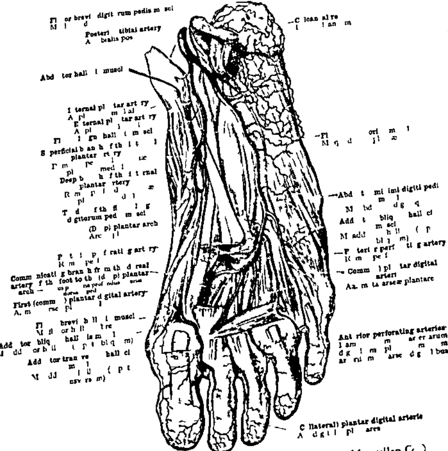


Fig. C — Arterial blood supply. Plantar [illegible] (T[illegible] courtesy The Macmillan Co.)

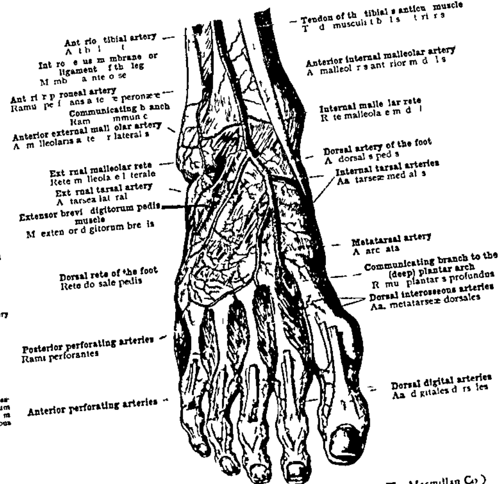
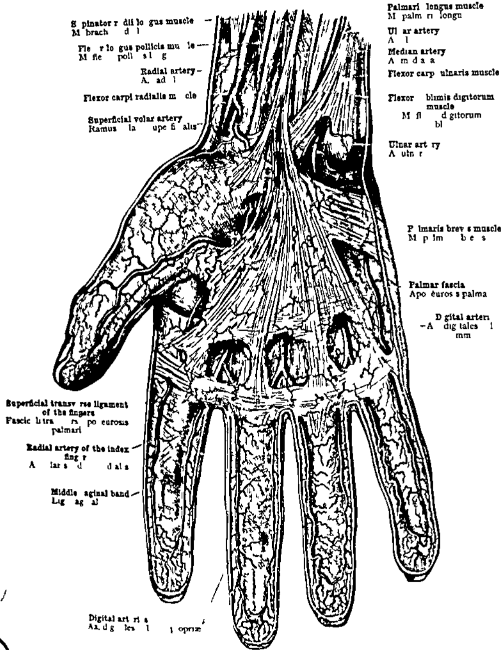
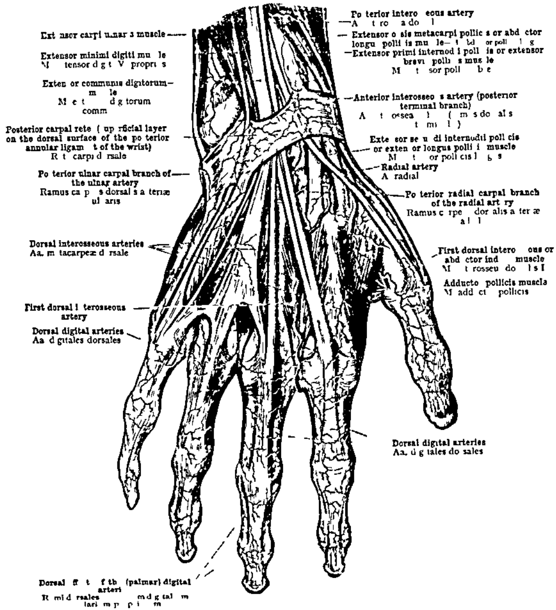


Fig. 1D — Arterial blood supply. Dorsal [illegible] (T[illegible] courtesy The Macmillan Co.)



Fi iA Arter l bl ood pply V l f g (T ld y Th M m ll n C)



F o B—A l bl ood pply D l f ng (T ld y Th M n C)

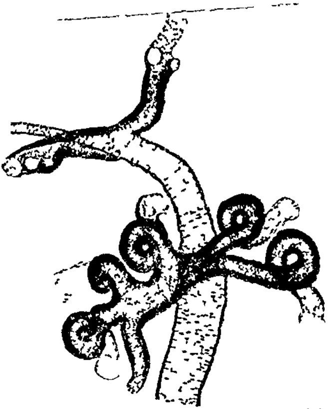


Fig C—Project on drawing (X 74) of a group of anastomoses in the nail bed of the toe The artery c ses the center of the drawing and gives rise to twelve thick walled anastomotic branches The th n w lled e o terminat ons of se eral are shown (Grant and Bl nd courtesy Clin cal Science)

may help to supply the dorsal parts of the proximal phalanges of the fingers and toes These arise from the radial and the dorsalis pedis arteries respectively These dorsal arteries are perhaps most distinct in the great toe (fig 1)

The major arteries of the fingers and toes divide into smaller arteries coursing toward the axis of the digit in a ladder like effect These in turn divide into arterioles penetrating all the tissues of the digits The most elaborate plexus is formed in the terminal segments The arterioles divide into capillary plexuses which supply the tissues of the fingertip directly with nutrition and oxygen from the blood stream Under the skin and nails however there are numerous coiled communications between arterioles and venules in the form of arteriovenous anastomoses The arteriole and arteriovenous anastomosis are distinguished from the capillary by the muscular coat which thins out in the glomus on the venule side [200] There are more glomera per square centimeter of surface area in the fingers and toes than in any other part of the body [200] They are highly innervated reactive muscular structures In the fingers there are from 250 to 500 whereas in the toe there are from 300 to 600 glomera per square centimeter (fig 2)

The capillaries themselves are not distinguishable from those in other



Fig 2A —Untouched photomicrograph (× 25) of portion of a vertical section (200 μ thick) through the pad of a toe The vessels and coiled sweat glands show up clearly against the faintly stained background Note the vessels of the subpapillary venous plexus standing out as though drawn In the center of the figure an artery turns toward the surface from the left it gives rise to a group of darkly stained anastomoses (A) the details of which are not visible Part of another group of anastomoses is to be seen in the middle of the extreme left of the figure (B) (Grant and Bland [2 0] courtesy Clinical Science)



Fig 2B —Untouched photomicrograph (× 300) of an arteriovenous anastomosis in the sole of the foot (from a section 200 μ thick) To the left of the figure an artery runs upward the nuclei of its circular muscle fibers are in focus at the top of the figure It gives rise to an anastomosis that coils on itself and passes to the right to widen out into a thin walled vein Note the numerous rounded nuclei in the thick wall of the anastomoses (Grant and Bland [2] courtesy Clinical Science)

also supplies the toes with some blood [10, 03, 463] There is one digital plantar artery on each side of each toe [673]

Both in the toes and in the fingers, rudimentary dorsal digital arteries

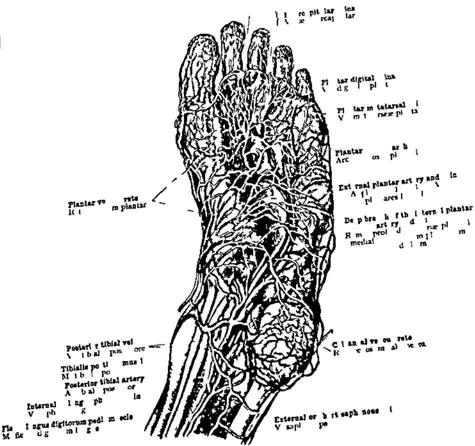


Fig 4A —Digital [illegible] Plantar [illegible] (T[illegible] The Macmillan Co)

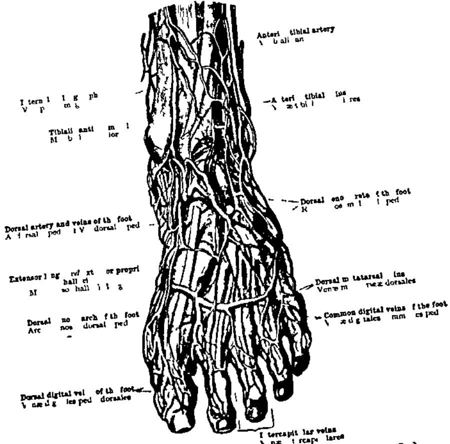


Fig 4B —Digital veins Dorsal [illegible] (T[illegible] The Macmillan Co)

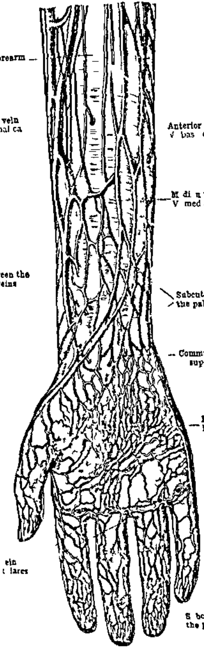


Fig. 3A – Digital ve ns V l r fi gers (T ldt c rte y The Macm llan Co)

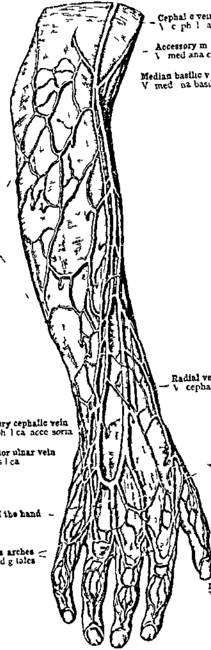


Fig. 3B — D g t l en D l f ge s (Toldt c rt y The M cm llan C)

2

PHYSIOLOGY

THE normal blood flow through the finger and toe may vary enormously. Flow rates as low as 0.01 cc/sq cm/min[401] and as high as 0.38 for the fingertip[391] and 0.29 for the toe[337] have been recorded in the normal subject. The reason for this enormous variation is the large number of arteriovenous anastomoses in the fingertip and toe, a major function of which is, by relaxation and constriction, the dissipation or conservation of body heat.[107, 214] It has been estimated that the metabolic requirements of the fingertip or toe demand one tenth or less of the blood supply received when the vessels are fully dilated.[1, 214] There is no known method, however, for the quantitative separation of capillary from arteriovenous flow.* After inhibition of sympathetic nerve discharge, blood flow at heart level through the finger varies from 0.25 to 0.38 cc/sq cm/min and that through the toe from 0.15 to 0.29 cc/sq cm/min.[33] The difference is probably due to the lower arterial and higher venous[441] blood pressure in the toe as compared with the finger. These data were obtained chiefly from calorimetric studies. With venous obstruction plethysmography, blood flow is expressed as cc per hundred cc of tissue volume. The normal range is of similar magnitude although somewhat wider because of technical difficulties[414] (p. 56). There is evidence of greater flow per unit of tissue in children and some correlation of vascular caliber with age may eventually be demonstrated.[illegible] The tremendous flow through digital arteriovenous anastomoses after inhibition of sympathetic nerve discharge is further

* The term "normal flow" is used throughout to indicate flow obtained after inhibition of sympathetic nerve discharge. A greater flow than this may, however, be obtained by additional capillary dilatation as produced by direct heat or cold,[illegible] reactive hyperemia,[illegible] or by chemical and hormonal stimulation.[illegible]

parts of the body they supply the skin, connective tissue tendon, and bone with blood. At the base of the nail the capillaries may be visualized as loops passing from the arterial to the venous side (p. 39).[17, 551]

The capillaries and glomera empty into venules which in turn drain into a plexus of veins these are for the most part immediately subcutaneous in contrast to the arteries which are somewhat deeper.[120, 203, 463] The venules are the chief source of the color of the fingers or toes especially under the nails where there is a rich uniform plexus.[24] The large veins at the base of the fingers or toes empty into the superficial veins of the hand or foot which in turn join with other veins to form the major venous channels of the upper or lower extremity.[120, 203, 463] In addition to the superficial digital venous plexuses there are bone veins and a deep periosteal plexus and also small venae comitantes which lie adjacent to the digital arteries.[120, 203, 463] There is usually one vein on each side of the artery with lattice like communicating branches crossing over and under the artery (figs. 3 and 4).[120, 203, 463, 573]

The arteries, veins and glomera are supplied with both afferent and efferent nerves.[37, 39, 56] The capillaries are probably not innervated directly.[6, 8] The motor nerves are sympathetic or adrenergic.[95] The effect of cholinergic or parasympathetic nerves on the digital circulation is questionable.[30, 534] The blood vessels of the fingers and toes are innervated by perivascular plexuses which receive numerous branches from major motor sensory and mixed nerves.[484] A more detailed discussion of nerve function and pathways will be found on page 12.

The lymphatics of the digits are not clearly defined channels except along the lateral aspects of the fingers or toes where a superficial and a deep system accompany the arteries and veins.[120, 203, 485] The tissue spaces themselves drain into superficial and deep lymphatic vessels which eventually join to form larger lymphatic conduits.

Anomalous blood supply to the fingers and toes is not uncommon.[120, 203, 463] The dorsalis pedis artery may be absent unilaterally or bilaterally.[47] One or more of the four arteries that supply a finger[615] or toe may be absent or rudimentary and their origin from the interosseous arteries and arches may be variable. The venous drainage is even more variable so that except for venae comitantes one can speak only of subcutaneous and deep venous plexuses rather than of well defined digital veins.[120, 203, 463] Lymphatic drainage is also subject to anatomic variation. Even the number of glomera per unit of skin varies although statistical data on this point are meager.[60]

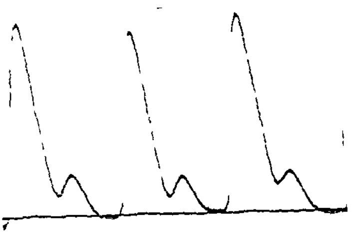


FIG 6 —Pulse wa e record ngs obtained from the d git f normals with a new type of oscill meter (c lograph) (Lax and Feinberg r repr duced with perm si n of authors)

of water and in the dorsum of the foot 19 cm of water [411] The higher values here than in more proximal veins may be attributable to the effects of arteriovenous anastomoses

The normal pulse wave contour in the digit is illustrated in figure 5 The curve is obtained by measuring the changes in digital volume with a recording plethysmograph [79] An anacrotic notch is rarely seen in the digit The dicrotic notch on the other hand is usually definite and usually occupies the position on the downstroke of the pulse contour as indicated in figure 5 The dicrotic wave may be seen more distinctly in records obtained with the recording oscillometer (fig 6) [337] The volume pulse contour may vary tremendously normally depending on the degree of vasoconstriction or vasodilatation encountered In general the amplitude of the volume pulse is related to the volume blood flow [55] [255] [258] although this relationship is not linear [11] Pathologic conditions such as aortic insufficiency may for example produce an increased amplitude of pulse without a corresponding increase in blood flow For comparative purposes pulse wave contours are best examined after inhibition of sympathetic nerve discharge [253] Their form is similar in many ways to the pulse curves obtained at the wrist with the sphygmograph [610]

The nervous control of the blood vessels of the fingertip and toe is exercised almost entirely by the sympathetic nervous system [17] [93] [330] [5] [6] [608] Stimulation produces constriction and inhibition of nerve discharge dilatation There may be further direct dilatation via cholinergic nerves [2] but if this occurs at all the effect is so small as to be practically immeasurable [594] Vasodilator activity can however be demonstrated in the more proximal parts of the systemic circulation [22] [201] and may be mediated via anatomically separate pathways [6] [5] Vasodilatation can also be produced by antidromic stimulation of sensory nerves [160] The nerve

documented by finding blood oxygen tensions, when measured oximetrically[11] or directly, to be very close to those of arterial blood.[11]

The blood pressure in the digital arteries[596, 380, 32] varies considerably less than does the blood flow with changes in sympathetic nerve discharge. When this discharge is not inhibited, the digital systolic blood pressure is 101 ± a standard deviation of 13 mm. Hg. The mean brachial digital systolic pressure gradient before inhibition of sympathetic nerve discharge is 19 mm. ± a standard deviation of 5.5 mm. If sympathetic nerve discharge is not inhibited, it is difficult to measure digital diastolic blood pressure consistently. After inhibition of sympathetic nerve discharge the mean digital systolic pressure is 96 ± a standard deviation of 9 mm. Hg. The mean diastolic pressure is 58 mm. Hg ± a standard deviation of 11 mm. The mean of digital arithmetic mean pressures is 80 mm. Hg ± a standard deviation of 8 mm., and of brachial digital arithmetic mean pressure gradients 18 mm. ± a standard deviation of 9 mm. Hg. The mean brachial digital systolic gradient is 15.9 ± a standard deviation of 7 mm. Hg and the diastolic gradient 19 ± a standard deviation of 11 mm. Hg.

In the toe[40] it is possible with available methods to measure only the systolic blood pressure. After inhibition of sympathetic nerve discharge the mean hallucal systolic pressure is 87 mm. Hg ± a standard deviation of 15 mm.

Mean venous pressure in the dorsum of the hand at heart level is 14 cm.

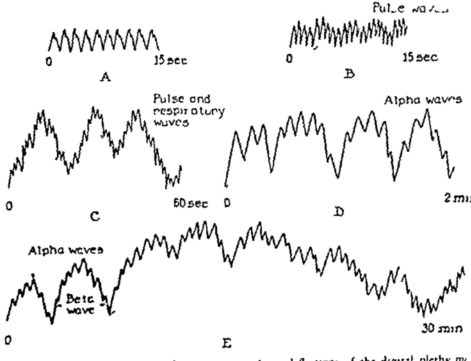


FIG. 5.—Diagram of five types of spontaneous volume deflections of the digital plethysmograph (Burch, Cohn and Neumann,[8] courtesy J. Clin. Investigation.)

vasoconstrictive [118] The secretion of the adrenal medulla contains a variable amount of norepinephrine ranging from 18 to 36 per cent [331] Ordinarily there is no epinephrine or norepinephrine circulating in the blood in assayable[390] amounts sufficient to affect vascular caliber During stress however such humoral vasoconstriction may be considerable [84]

Other vasoconstrictive substances are alleged to affect vascular caliber via the blood stream Epinephrine like substances[335] elaborated by nerve endings[86] may sometimes it is believed be absorbed to act humorally again only under conditions of great stress Vasoconstrictive substances derived from the kidney such as angiotonin [114] hypertensin [116] renin [48] VEM [319] and pherentasin [47] and from the brain and blood such as serotonin [369] all produce humoral vasoconstriction although their demonstration in the blood of hypertensive patients has been inconsistent [471] [444] and quantitatively not commensurate with the extent of the humoral phase of the hypertension Some of these substances are alleged to be rapidly changed in the tissues by enzymes to inactive states [114] [116b] Because of the controversial views on their function judgment as to the physiologic importance of these pressor agents must be suspended

No other circulating physiologic substances have a direct effect on vascular caliber Adrenal cortical steroids may affect vascular reactivity [472] but it is the prevailing view that the major effect is indirect via the hormone s action on the kidney and on fluid and electrolyte balance [118]

In addition to humoral and nervous control there is some evidence that local factors may exercise basic control over vascular caliber [382] These local factors may be influenced by various local and general metabolic changes Local injury [37] for example releases H substance which provokes the triple response of Lewis [341] [24] The H substance is probably not histamine [84] A factor in addition to caliber which affect flow locally is that of blood viscosity [35] [39] Our knowledge of the effects of these factors is fragmentary and often obscured by nervous and humoral effects

Generally increase in metabolism increases capillary blood flow and decrease in metabolism produces an opposite effect [371] In the fingertip however hypermetabolism decreases heat conserving sympathetic vasoconstriction because of the generally increased heat production This raises the average digital blood flow to something nearer the maximum [401] [3] [9] The maximum blood flow itself is not measurably increased because capillary circulation represents 10 per cent or less of the total blood flow and an increase of 50 per cent in this fraction would produce only a 5 per cent increase in total blood flow Hypometabolism produces an effect directly opposite but maximum blood flow again is not measurably decreased [401]

The effects of increased hydration and dehydration are also largely on capillary rather than arteriovenous blood flow [16] [810] Dehydration probably produces vasodilatation and hydration vasoconstriction Increased

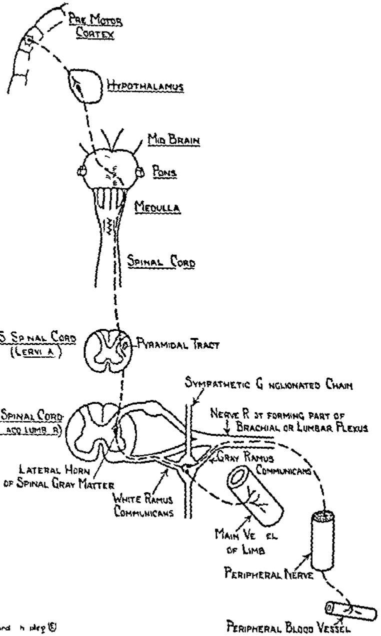


Fig. 7.—Diagram of sympathetic vasomotor pathways to limbs (Richards[illegible], courtesy E. and S. Livingstone, Ltd.)

pathways[489] concerned with vasoconstriction and dilatation[210, 21] are depicted in figure 7.

Another way in which the caliber of blood vessels may be affected is by substances circulating in the blood capable of producing vasoconstriction and vasodilatation.[609, 619] Such humoral control of vascular caliber is superimposed on the nervous control, the resultant determining the actual dimensions of the vascular bed. Of the physiologic substances capable of such action the best known is epinephrine.[12, 216] This has been recently differentiated from norepinephrine[559] which is thought to be largely

tissue pressure with hydration may add the factor of vascular compression These effects are less demonstrable on maximal digital blood flow through arteriovenous anastomoses It can be shown, for example that increased hydration, as produced by unilateral lymphedema has no significant effect on maximal digital blood flow (table 1) [101] There is some evidence, however that changes in tissue electrolyte concentration may play a role in the determination of intrinsic or non neurogenic vascular caliber [1??]

Hyperoxemia and anoxemia probably al o produce vasoconstriction and vasodilatation respectively in the capillary bed[24] although this may be obscured by reflex effects [23] The effect on flow through arteriovenous anas omoses is probably minimal (p 243) Anoxia produced by arterial obstruction results in characteristic reactive hyperemia [31 ? 232 635] Changes in blood viscosity do not influence vascular caliber despite their effect on resistance [391 ??] This is more fully discussed on page 8_

Emotion affects the blood vessels of the digits chiefly via the sympathetic nervous system although under extreme stress circulating nor epinephrin may also play a role in vasoconstriction [46] Adrenocortico tropic hormone (ACTH) and cortisone produce more prolonged effects and may influence vascular reactivity [471] as well as fluid and electrolyte balan e [? ?] Pulse volume curves obtained with the digital plethysmograph reveal regularly recurring waves of sympathetic nerve discharge [? 19] superimposed upon pulse waves and respiratory waves (fig 5) [15 22] Th e aves are usually independent of changes in pressure in the more p oximal arteries [193]

Generally pleasurable emotions inhibit sympathetic nerve discharge [? ??] and unpleasant emotions[155] such as fear[??] or sensations[109] such as pain [?] increase it [?] Reflex vasospasm can also be produced by electrical stimulation [?] o by t auma to arterial adventitia [??8] Sympathetic nerve discharge is inhibited by satisfactory sexual experience and also by sleep [?] Intellectual or physical effort usually increases nerve discharge except if increased heat production outweighs the effect of effort [? ??] Sweating is usually an accompaniment of complete inhibition of sympathetic nerve di charge by heat (p 47) but under severe emotional stress it may accompany vasoconstriction [317] Such cold sweat is especially prominent in the extremities and face but may be generalized The nerve pathways for sweating[53 ? 31 ???] are illustrated in figure 7 The distribution of vasomotor and sudomotor fibers however is not necessarily the same [? 16] and the sudomotor fibers may be both cholinergic and adrenergic [? 31]

Heat and cold have specific effects on the digital circulation [?] One of the chief functions of th arteriovenous anastomoses is that of heat regulation Generally hea applied to the body as a whole inhibits sympa

TABLE 1 The Measurement of Digital Blood Pressure, Flow and Vascular Volume Index in Both Upper Extremities of Patients with Unilateral Lymphedema (Mendlowitz[101])

Pt	Age and sex	Diagnosis	Brachial B.P. (mm Hg) lt	Brachial B.P. (mm Hg) rt	Digital B.P. (mm Hg) lt	Digital B.P. (mm Hg) rt	Blood flow (cc/cm³/min) lt	Blood flow (cc/cm³/min) rt	Vascular volume index/cm³ of skin (cu µ) lt	Vascular volume index/cm³ of skin (cu µ) rt
R F	26 F	Thrombosed axillary vein rt with residual lymphedema	100/68	100/68	60/48	64/48	0.45	0.40	1688	1501
L B	[illegible] F	Lymphedema rt hand and both feet. Etiology ?	112/58	110/60	68/55	70/30	0.37	0.44	1218	1519
H S	49 F	Rt radical mastectomy for ca rt breast. Bilat. mild arthralgia both hands. Moderate lymphedema	122/84		96/56	96/56	0.26	0.29	[illegible]	750
M W	69 F	Rt radical mastectomy for cirrhous ca of breast	150/8[illegible]	158/86	106/46	32/54	0.34	0.30	986	844
H M	55 F	Rt radical mastectomy for ca rt breast. Marked lymphedema	108/66	128/89	96/72	68/54	0.41	0.34	949	1162
P W	39 F	Lt radical mastectomy for scirrhous ca	99/68	96/72	70/36	76/56	0.33	0.33	1317	1032
A N	39 F	Lt mastectomy for cirrhous ca lt breast	98/70	102/64	66/40	62/38	0.30	0.32	1125	1332
A C	51 F	Lt radical mastectomy for ca left breast. Lymphedema slight	136/94	15[illegible]/84	88/56	96/62	0.35	0.26	965	675
R D	44 F	Left radical mastectomy for cirrhous ca lt breast. Lymphedema very slight	118/94	124/96	96/70	94/72	0.28	0.35	700	844
A B	[illegible]5 F	Rt mastectomy for ca rt breast. Lymphedema minimal	120/76	118/72	86/64	84/58	0.33	0.33	952	937
C M	59 F	Lt radical mastectomy for ca lt breast. Lymphedema minimal	142/82	146/78	98/51	90/48	0.37	0.36	978	1069
D G	43 F	Lt radical mastectomy for ca lt breast. Lymphedema marked	98/60	106/66	74/38	72/36	0.40	0.34	1443	1294
A L	58 F	Lt radical mastectomy for scirrhous ca lt breast. Lymphedema slight to moderate	108/74	114/[illegible]	90/62	9[illegible]/60	0.33	0.33	897	882
S W	51 F	Lt radical mastectomy for scirrhous ca lt breast. Lymphedema moderate	104/64	110/68	100/62	94/38	0.36	0.37	877	1162

SC 1950[114] are even more effective than TEAC in blocking sympathetic impulses traversing the ganglia (p 19) Hexamethonium seems more effective in the lower than in the upper extremities [86] In the lower extremities procaine nerve block combined with direct heat produces the greatest degree of vasodilatation [62] The latter however, affects the patency of capillaries directly as well as sympathetic nerve discharge

Posture has an effect on the digital circulation especially in the lower extremities [190, 394] Theoretically hydrostatic pressure changes[465, 504] should be the same in arteries and veins[4, 5, 6] thus cancelling out as far as effective pressure and flow through the tissues is concerned This is modified by the venous pumping action of exercise [488] the effect of the valves and also by sympathetic nervous reflexes in response to postural changes [45, 610] These reflexes constrict the veins and the arteries as hydrostatic pressure increases If they are interfered with by disease sympathectomy or blocking drugs postural hypotension may occur in the upper part of the body with resultant syncope [48, 610] At heart level the digital circulation after inhibition of sympathetic nerve discharge is however often normal in such cases [401]

thetic nerve discharge,[139, 461] whereas the withdrawal of heat from the body as a whole increases sympathetic nerve discharge.[9, 316] The effect is believed to be reflex from the heated area, although some hold that the warmed or cooled venous blood acts on affectors in the brain or elsewhere.[275, 469] It is possible that warmed or cooled venous blood, and hence arterial blood (p. 69), by heating or cooling the skin in regions other than those externally heated or cooled, accelerates the process of decreasing or increasing sympathetic nerve discharge.[9]

Complete inhibition by indirect heat of sympathetic nerve discharge in the upper extremity is usually heralded by the onset of sweating, a response of the body to positive heat balance.[484] In the toe, similar inhibition is occasionally incomplete[461] and may require $1\frac{1}{2}$ hours of heating[40] as against 20 to 30 minutes for the upper extremity.[461] It should be pointed out that sympathetic vasoconstriction is capable of easily breaking through the inhibition induced by heat.[418] This "break through" is made more difficult by ganglionic blocking drugs such as tetraethylammonium chloride (TEAC) and the hexamethonium compounds.[401, 413] A comparison of the effects of spinal anesthesia[25, 27, 81, 4, 4, 53] with those of heat and TEAC on the circulation in the great toe measured calorimetrically (table 2) indicates that, at least in the skin of the great toe, heat and TEAC produce complete inhibition of sympathetic nerve discharge.[07, 413] There is some evidence that this inhibition is less complete for deeper blood vessels.[272, 413, 6, 3] The hexamethonium compounds[136, 455] and

TABLE 2.—*The Effects of Indirect Heating and TEAC Compared with the Effects of Spinal Anesthesia or Sympathectomy on the Circulation of the Great Toe (Mendlowitz, Touroff and Abel[4, 8])*

Patient	Age and sex	Indirect heating and TEAC: Brachial blood pressure (mm. Hg)	Indirect heating and TEAC: Blood flow (c.c./sq. cm./min.)	Spinal anesthesia or sympathectomy: Dosage pontocaine	Spinal anesthesia or sympathectomy: Brachial blood pressure (mm. Hg)	Spinal anesthesia or sympathectomy: Blood flow (c.c./sq. cm./min.)
1	28 M	130/80	0.15	13 mg	143/85	0.15
2	60 M	128/100	0.19	20 mg	100/80	0.12
3	15 M	108/64	0.25	8 mg	118/60	0.08
4	59 F	204/84	0.14	12 mg	160/90	0.14
5	66 M	132/60	0.15	15 mg	95/75	0.10
6	48 F	108/64	0.18	16 mg	100/70	0.14
7	55 F	96/70	0.16	15 mg	95/[illegible]	0.19
8	42 M	92/76	0.21	16 mg	110/[illegible]	[illegible]10
9	24 M	88/[illegible]	0.14	15 mg	90/60	0.15
10	44 F	112/[illegible]	0.23	15 mg	85/[illegible]	0.17
11	29 M	82/52	0.15	16 mg	80/50	[illegible]
12	29 M	116/80	0.15	12 mg	108/[illegible]	0.20
13	22 M	130/90	0.21	2 days after sympathectomy	110/[illegible]	0.19

pathways for stimulation of the autonomic nervous system whereas the moderator nerves from the aorta and carotid sinus are inhibitory [44, 64]. Systemically administered procaine would theoretically [51] have the effect for example of blocking sensory impulses via these routes [311] and any drug producing a pleasurable sensation or warmth would have a similar effect.

On the motor side blocking drugs may act at different synapse levels. In the cerebral cortex the barbiturates [176], alcohol [112, 193], the anesthetics [5, 31, 305] and narcotics [311] all interfere with autonomic discharge in addition to their other effects. *Rauwolfia serpentina*[580] also probably acts on the cortex and possibly on the subcortical centers as well.

It is at the hypothalamic synapse level that such drugs as the hydrogenated ergot derivatives [189, 191, 56], the veratrum alkaloids [111, 112, 31] and 1 hydrazinophthalazine[406] have their chief blocking effect. The effectiveness of these drugs is usually limited by their side actions and the development of tolerance. The only drugs known to be capable of blocking a third motor synapse level in the spinal cord are those used for spinal anesthesia such as procaine [311].

The fourth motor synapse level in the autonomic ganglia themselves can be blocked by a recently developed group of compounds. These include among others [4, 49, 263, 244, 50, 573] tetraethylammonium salts such as tetraethylammonium chloride (TEAC) [17, 191, 416, 574] quaternary amines (SC 1950) [114] and penta and hexamethonium salts [84, 156, 154, 504]. The rate of excretion by the kidney of these drugs determines the duration of their effect and is most rapid for TEAC and slowest for the methonium compounds.

The sympathetic nerve endings may be blocked by such agents as dibenamine [35, 50, 423] and dibenzyline (SKF 688 A) [26, 484, 427, 410] as well as by imidazoline compounds (priscoline) [223]. The former two drugs which are more constant in their effect when parenterally rather than orally administered also block the action of circulating epinephrine and norepinephrine on these nerve endings. The most effective agents for this purpose however are piperoxan (benzodioxane)[14, 156] and another imidazoline compound (regitine) [147, 88] and these drugs are often used to test for the presence of an actively secreting pheochromocytoma. When used for this purpose piperoxan may occasionally produce hypertension and alarming tachycardia [414, 616]. Drugs blocking parasympathetic nerve endings such as atropine and scopolamine affect the digital circulation only indirectly by reflex action or by psychologic response to their direct actions [311].

The nitrites [17, 193, 492, 545, 598] and the xanthine group of drugs (theophyllin)[19, 495, 439] inhibit the tone of the smooth muscle of blood vessels directly whereas 2 benzyl imidazoline hydrochloride (priscoline) [22], histamine [155, 193, 339] and nicotinic acid[311] have direct dilating actions on

3.

PHARMACOLOGY

DRUGS of various types act on the digital blood vessels[198, 400, 498, 539] producing for the most part either vasoconstriction or vasodilatation. A drug may also cause an increase or decrease in effective digital arterial blood pressure, thus producing increased or decreased digital blood flow apart from its effect on the caliber of the blood vessels. Decreased digital arterial blood pressure may, for example, occur whenever a vasodilating drug produces postural hypotension. The effect of the drug on flow in the fingers may thus be out of proportion or opposite to its effect on systemic blood flow as a whole.[401] Sudden ganglionic blockade, as caused by the intravenous injection of hexamethonium compounds, may in addition decrease arterial blood pressure, including digital pressure, to shock levels without producing tachycardia,[465] simply by distending the vascular system beyond the capacity of the blood volume to fill it adequately. The significance of these effects may not be recognized unless blood pressure, flow, and vascular resistance are measured simultaneously.[401]

The pharmacodynamics of drugs acting on the digital circulation are complex.[311] These drugs may be classified according to whether they block the chain of reactions which produces vasomotor tone, thus causing dilatation of peripheral blood vessels (table 3),[400, 437, 438] or stimulate these reactions and thus constrict these vessels (table 4). They may in addition be subclassified according to the site of their major effects on the reaction complex which determines vascular caliber (fig. 7).

Although not commonly used as vasodilators, there are drugs which act on the sensory inflow to the system of relays ending in the final common pathway of the autonomic nervous system. Sensory nerves in general are

pathways for stimulation of the autonomic nervous system whereas the moderator nerves from the aorta and carotid sinus are inhibitory [55, 144] systemically administered procaine would theoretically [4] have the effect, for example of blocking sensory impulses via these routes [311] and any drug producing a pleasurable sensation or warmth would have a similar effect

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The fourth motor synapse level in the autonomic ganglia themselves can be blocked by a recently developed group of compounds These in clude among others [4, 43, 262, 281, 50, 374] *tetraethyl*ammonium salts such as tetraethylammonium chloride (TEAC) [15, 191, 419, 4??] quaternary amines (SC 1950) [114] and penta and hexamethonium salts [55, 144, 154, 308] The rate of excretion by the kidney of these drugs determines the duration of their effect and is most rapid for TEAC and slowest for the methonium compounds

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TABLE 3 —*Blocking Drugs* (*Mendlowitz*[401])

Drugs	Site of action	Block	Mode of administration	Dosage	Duration of effect	Major side actions	Tolerance
1 Procaine	Sensory and moderator nerves	Sympathetic + Parasympathetic +	i v	Variable		Collapse	
2 Barbiturates bromides other hypnotics narcotics and anesthetics	Cerebral cortex	Sympathetic ++ Parasympathetic ±	p o p h i v inhalation	Variable		Somnolence respiratory depression	++
3 Veratrum alkaloids (Protoveratrine) (Veroxin	Hypothalamus	Sympathetic ++ Parasympathetic ±	p o i v i m	1–3 mg t i d 1–3 mg	Moderate	Nausea *vomiting cardiotoxic?*	+
4 1 hydrazino phthalazine	Hypothalamus Capillaries	Sympathetic +++ Parasympathetic ± Capillarie ++	p o	50–200 mg q 4 h	Moderate	Leg edema postural hypotension nausea vomiting drug fever psychosis headache nasal congestion joint pains skin eruption	+
5 Hydrogenated ergot derivative (Hydergine	Hypothalamus	Sympathetic +++ Parasympathetic *o*	i v i m s l	0 3 mg 0 3 mg b i d 0 3 mg t i d	Moderate	Postural hypotension nasal congestion nausea	+
6 Procaine	Spinal cord	Sympathetic +++ Parasympathetic +	i s			Collapse	

Tetraethylammonium salt (TEAC)	Autonomic ganglia	Sympathetic +++ Parasympathetic +	i v i m	5 mg/kg 10 mg/kg	Short	Tingling, paralysis of accommodation, postural hypotension, nausea, vomiting, shock	
8 Quaternary amine (SC 950) (Pendiomid)	Autonomic ganglia	Sympathetic +++ Parasympathetic ±	i m	5 50 mg 5 50 mg t i d	Moderate	As above except for tingling	
9 Penta and hexamethonium salts	Autonomic ganglia	Sympathetic ++++ Parasympathetic ±	i v i m p h p o	5 50 mg 5 50 mg b i d 250-1000 mg q 4 h	Long	As above, relative bradycardia, postural hypotension and collapse. Bromism if bromide salt is used. Oral preparation causes constipation and may cause paralytic ileus	
10 Methantheline bromide (Banthine)	Autonomic ganglia Autonomic nerve endings	Sympathetic + Parasympathetic +++	p o	50 100 mg q 6 h	Moderate	Nausea, vomiting, bladder paralysis?	
11 Dibenamine	Autonomic nerve endings	Sympathetic ++ Parasympathetic 0 Circulating epinephrine and norepinephrine ++	p o i v	5 mg/kg t i d 4 6 mg/kg	Moderate	Postural hypotension, nasal congestion, nausea, vomiting	++
12 Dibenzyline (SKF 688A)	Autonomic nerve endings	Sympathetic ++ Parasympathetic + Circulating epinephrine and norepinephrine ++	p o	20-60 mg t i d	Moderate	Postural hypotension, nasal congestion, nausea, vomiting	++

TABLE 3—*Continued*

Drugs	Site of action	Block	Mode of administration	Dosage	Duration of effect	Major side actions	Tolerance
13 V D M (*Ferritin*)	Autonomic nerve endings	Sympathetic + Parasympathetic 0 Epinephrine +					
14 Piperoxan (Benzodioxane)	Autonomic nerve endings	Sympathetic ± Parasympathetic 0 Epinephrine ++ *Norepinephrine* ++	i v	10 mg /sq m	Short	Hypertension and tachycardia	
15 2[(m hydroxy N p tolylanilino) methyl 2 imidazoline (Regitine)	Autonomic nerve endings	Sympathetic + Parasympathetic 0 Epinephrine ++ Norepinephrine ++	i v i m	5 mg	Short		
16 Atropine group	Basal ganglia autonomic nerve endings	Sympathetic 0 Parasympathetic +++	i m p h p o	Variable	Moderate	Dry mouth mydriasis excitability	
17 Nitrites	Smooth muscle of arterioles	Sympathetic ± Parasympathetic ± Smooth muscle ++	p o	60 mg (sod nitrite) t i d	Moderate	Headache collapse nausea and vomiting	
			inhalation	Amyl nitrite Perles			
			s l p h	Nitroglycerine 0 6 mg			

18 X thn g p (Th phyll Am n phyll n	Sm h m l f r c l pllae alt d te balas (d)	Sy p thet ± P s ympathe c ± Sm o h m le + Capilla +	p pp	0 2 0 4 Gm t d 0 25 Gm 0 5 Gm	M der t	C ll p e (r ely)
19 Ade c c ph ph t	Sm sh ma l f a te l le he re	Sympathetic o Par ympath t c o Smo th m s l ++	i m i		Sh r	Card ?toxic?
20 ben yl m da zol ne hydrochl d (P iscoli e)	A t n m c n rd ing and cap llar	Symp thet c + P r ymp thet o Capilla ie +++	i a p o	25 50 mg 50 mg 25 50 mg q 4 h	M derate	Tingl ng e ythema nau ea
21 H st mine	Cap ll r e	Sympathetic ± Para ympathet c ± Capilla es ++++	p h i a	0 05 mg 0 1 mg 0 05 mg	Sh rt	Headache h ck ga tric hyperacidity
22 Thi cyanate	Cap llarie ? Salt and ater balance? Ox d t ve enzymes	Symp thetic ± Para ympathet c ± Cap lla ie +	p)	0 3 mg t i d (Blo d le el sh uld n t exceed 12 mg %)	Mod rate	Agran l cyt s gl it s g ngi iti encephalit s
23 Merc r ial di re tics Exchange re in	Cap llar es ate and ale balance—k dney	Indirect	i m i v p h	1 2 cc	Long	Lc v salt syndrc me sh ck mercur l into icati n (rare)
24 Dig tal s group	Hypothalam heart smooth mu cle f enules and arteri les kidney (diure is) cap-llaries, water and salt balance	Sympathet c ± Parasympathetic + Smooth mu cle + Capillaries + Ind rect	p o i	Variable	Long	Arrhythmias na sea om iting s mn lence

TABLE 4 —*Stimulating Drugs (Mendlowitz*[401]*)*

Drugs	Site of action	Stimulation	Mode of administration	Dosage	Duration of effect	Side actions	Tolerance
1 Caffeine	Cerebral cortex	Parasympathetic + Sympathetic +	p o i v	0 2–0 3 Gm 0 3 Gm	Moderate	Headache agitation	++
2 Nikethamide (Coramine)	Cerebral cortex	Sympathetic + Parasympathetic ±	i v	0 3–0 5 Gm	Moderate	Agitation	
3 Amphetamine	Cerebral cortex autonomic nerve endings	Sympathetic + Parasympathetic 0	p o i v	5 mg b i d 10 mg	Moderate	Agitation insomnia tachycardia anorexia	
4 Nicotine	Hypothalamus autonomic ganglia	Sympathetic ++ Parasympathetic ++				Nausea vomiting peripheral vasospasm superimposed thrombosis	++
5 Strychnine	*Spinal cord*	Sympathetic + Parasympathetic 0				Tonic convulsions	
6 Methacholine hydrochloride (Mecholyl)	Autonomic nerve endings	Sympathetic + Parasympathetic ++ ++	i m	25 mg	Short	Collapse	
7 Norepinephrine	Autonomic nerve endings cerebral cortex	Sympathetic ++++ Parasympathetic 0	i v	10–20 µg / kg /min	Short	Headache	
8 Epinephrine	Autonomic nerve endings heart and bronchi cerebral cortex	Sympathetic +++ Parasympathetic 0	p h	1 mg	*Short*	Tachycardia bronchial dilatation tremor	

Drugs provocative of secretion of epinephrine and *nor epinephrine from adrenal medulla* and e*specially from* pheochromocytoma are Methacholine hydrochloride (Mecholyl) 25 mg i m histamine 0 05 mg i v and tetraethylammonium chloride 200–500 mg i v

9 Ephed	A tonom n e end ng c reb l c r	Sympath c ++ Pa a ymp th	p o	25 50 mg q 4 h	M d ate	T chyca d a g tat n tremor	
N o y ephr ne	A to m c ner e endi g cbral c r	Sympath t c ++ P r ympathetic o	1	5 o mg	M derate	Headache tremor	
11 Ang ot n n re n pherenta n tyr mi e eror mn VEM							
12 Ergot derivati es (Ergotamine) (Erg t ox n)	A t nomic ner e endi g smooth mu cle	Symp thet c (blocking) P r ympathet c o Sm th mu cle +++					
13 P tres in	Sm oth mu le cap llaries	Smooth mu cle ± Cap llaries ++	i m	10–20 units	Moderate	Coronary pa m	+
14 Ant histam n es (Chlortrimeton) (Pyriben am ne)	Capillaries	Cap llar es ++	p (	4 mg q 4 h 50 mg q 4 h		S mn lence	
15 Ad e cortic tr phic hormone Cor tisone Deso yc r ticosterone acetate	Ti s e metabolism renal excretion of sodium and ater vascular reactiv ity	Sympathetic + Parasy mpathetic o	p i m	Variable		D abetes heart failure hyperten ion	

the capillaries Salt depletors, such as mercurial diuretics and exchange resins as well as *thiocyanates may influence* vasomotor tone because of their effect on salt and water balance in the tissues [198, 311, 498, 539] Digitalis has a similar effect in the presence of heart failure, although this may be obscured by *an opposing tendency to constrict small arteries and* venules [295a, 311]

Theoretically, stimulating drugs should be found which act at every level in this complex system as counterparts to the blocking drugs Any drug may act on the sensory side if it causes pain or coldness or reflex inhibition of the moderator nerves Acting at the cortical level are such drugs as caffeine, amphetamine, and nikethamide [311] Stimulating drugs acting on the hypothalamus are not well defined and it is not known whether strychnine also stimulates spinal outflow to the sympathetic nervous system [311] A search is now proceeding for drugs capable of stimulating the autonomic ganglia directly Nicotine in small doses stimulates the central nervous system centers for vasoconstriction as well as the sympathetic ganglia [198, 311, 498, 539] In larger doses the synapses are blocked Smoking may cause inspiratory reflex vasoconstriction[6] and mental conditioning which results in vasoconstriction[401] apart from the action of absorbed nicotine Large amounts of nicotine must be absorbed by smoking before a vasoconstrictive effect becomes apparent especially in the tolerant subject [49, 631]

The most commonly used substances for stimulating the sympathetic *nervous system however are the so called sympathomimetic* drugs acting on the sympathetic nerve endings [198, 498, 539] These drugs have additional stimulating effects on the cerebral cortex Epinephrine and norepinephrine are the most potent in this group and there are many drugs which mimic the effect of these hormones (table 4) [316] Drugs causing stimulation of parasympathetic nerve endings and other parts of the central and sympathetic nervous system [198, 19, 311, 498, 539] such as acetylcholine pilocarpine neostigmine (prostigmine) and others have no direct effect on vasomotor tone but may have indirect reflex as well as psychologically induced effects on the caliber of blood vessels

Certain drugs may produce *vasoconstriction indirectly by stimulating* the adrenal medulla to secrete epinephrine and norepinephrine [17] They are particularly potent in this respect if there is a pheochromocytoma which is capable of secreting sufficient amounts of these hormones to dominate the vascular reaction pattern ordinarily established by the administration of these drugs Methacholine chloride (mecholyl) [193, 2] histamine[193, 491] and tetraethylammonium chloride[17, 221] have this property and are frequently used as provocative tests for the presence of such tumors

There are also drugs which have direct stimulating actions on blood vessels Ergot for example has a direct constricting action on the smooth muscle of arterioles [97] in addition to its other actions [195, 496, 539] This effect together with secondary thromboses may produce gangrene[453] or muscular contractures[108] in the digits The antihistaminics[311] cause direct capillary constriction but act chiefly when histamine or similar substances elaborated in the tissues have produced prior capillary dilatation

Adrenocorticotropic hormone[4, 5, 433] and the adrenal cortical hormones such as desoxycorticosterone acetate[361] and cortisone [418, 536] may produce vasoconstriction directly because of their effect on the reactivity of blood vessels to stimulation by sympathetic discharge or by circulating epinephrine or norepinephrine or indirectly because of their influence on salt and water retention [454, 473] If salt is restricted however they appear to have no significant effect on non neurogenic or intrinsic digital vascular resistance [481] Any drug producing shock will also indirectly decrease digital blood flow not only by reflex vasoconstriction[144, 308] but also because of a decreased head of pressure in the digital arteries [401]

4

PATHOLOGY

Morbid anatomy of the digital circulation has not been extensively studied, the chief reason being the limited permission for prosection usually obtained. Also many abnormalities affecting the digital circulation, such as infections, are acute conditions which yield to therapeutic measures and are rarely observed pathologically. This chapter will touch on those anatomic changes produced in the fingers or toes by disease which have been studied pathologically. Much of this material will be reconsidered from the point of view of pathogenesis in the chapters on the effect of these separate diseases on the digital circulation.

Sir Thomas Lewis and his co-workers carried out extensive studies on the pathologic changes in digital vessels in Raynaud's disease and came to the conclusion that the disease is due to a fault in these vessels.[348] This fault consists either of arteriosclerosis or more often of thrombosis or the later effects of thrombosis with intimal thickening, recanalization, or even obliteration (fig. 8). Narrowing can also often be demonstrated by angiography during life.[16, 6] In cases of early Raynaud's disease these changes are more difficult to find. Secondary scleroderma is a late sequela.

The digital changes in primary scleroderma are fairly well documented and in general consist in the laying down of subcutaneous connective tissue scar.[444, 447] In thromboangiitis obliterans[75, 493] digital tissue alterations are secondary to arterial thrombosis and in the skin may range all the way from minimal cutaneous necrosis with resulting sclerosis to gangrene. The pathologic features are most pronounced in the epidermis, although secondary scleroderma is also seen. In trench foot and frost bite, intravascular sludge and arterial thrombi are often found (fig. 9).[17, 312, 349]

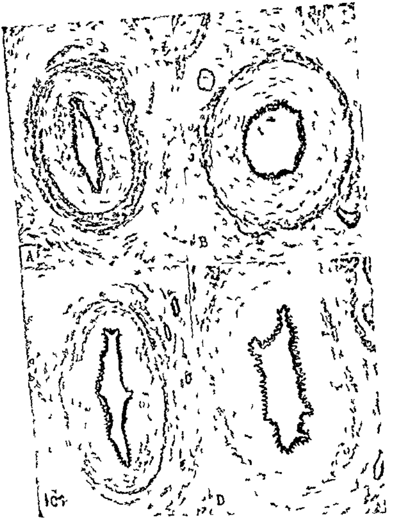


FIG 8 – Digital arteries in Raynaud's disease (Lewis[3?] courtesy Clinical Science)

(A) A woman of 14 years. Warm hand. Digital artery near end of fourth left finger. Almost if not quite normal. Weigert's stain.

(B) A man of 39 years. Warm hands. Digital artery near end of fourth left finger. Slight thickening of intima. Weigert's stain.

(C and D) Raynaud's disease in older form. Digital arteries at base of right second finger (C) and at middle of right fourth finger (D). There is slight patchy thickening of the intima. Weigert's stain.

Ice crystals can be demonstrated in the tissues in frost bite only. In trench foot[1 ... 8 9] or immersion foot[40] scar tissue is often laid down in muscle and subcutaneous tissue causing contracture and presumably compression of vessels (fig 10)

The fact that clubbing consists of tissue hyperplasia and hypertrophy[265 266 ... 95] is demonstrated in figure 11. Histologic and radiographic injection studies of the vessels moreover by Lovell[264] and also by Charr

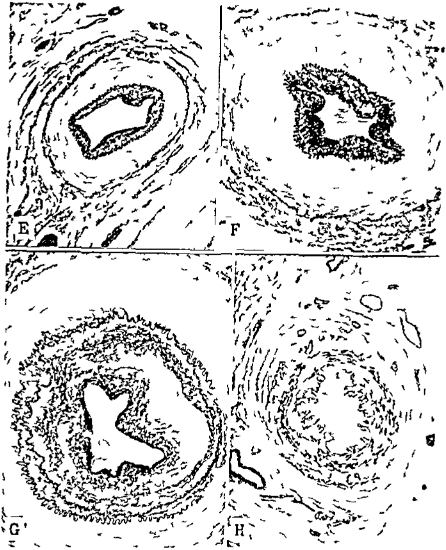


Fig 8 *Cont d*

*(E) Warm hand Digital artery near end of left index finger to illustrate moderate general hyper*plasia of the intima Weigert s stain

(F) Raynaud s disease aged 44 uncomplicated Digital artery from the right index finger Adventitia and media show little abnormality The intima is moderately and generally thickened Weigert s stain

(G) Palmar artery showing conspicuous thickening of intima The elastic lamella is broken to the right Weigert s stain

(H) Raynaud s disease severe form Digital artery from base of fourth right finger The lumen obliterated by almost homogenous sparsely enucleated connective tissue Hematoxylin and eosin

and Swenson [101] showed them to be dilated over the normal (fig 12) The pathologic effects of hypertension on the digital vessels have not been studied

The glomus tumor is an uncommon but readily recognized lesion found chiefly in the digit It has been extensively studied pathologically [376 468] (fig 13) and consists of a vascular neural anomaly developing at the site of an arteriovenous anastomosis

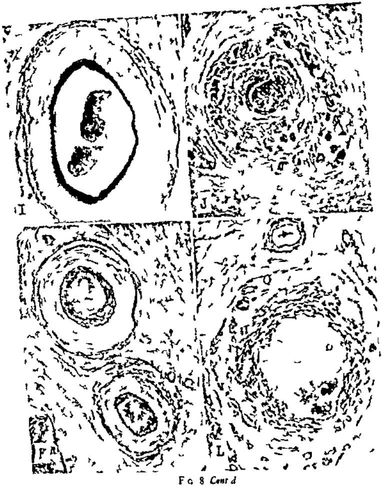


Fig 8 Cont'd

(I Ray aud s disease aged 53 milde t form Dilated d gital rtery near the middle cf left index finger show ng sl ght hyperpl a of th intima Weigert stain

J An tery nea end of ight i d x finger The thick ad entitia is fibrous and vascular The inne cor onta n a th l yer of m dial m scle cells rec nalised and enclosing a dense fibrous plug to one de of wh ch em ins of th main el tic l m a are i ible Hematoxyl n and eosin

K Ray a d s di e se se ere form Dig tal artery near end of right third finger has di ided into eq allv effe ti e br ches A th n ad entit a and well de eloped media The lamella is well defined though br ken n me place Lumen almost bl cked by th ckened int ma richly elastic in its outer more c ll la n it er laye s Weigert s t in

(L Ray ud dise se se e e form Digital artery from base of amputated finger Ad entitia and med a well defined both r canalised Elastic l mell w ll defined Within it the artery is block d by alm st homoge ou fibrous ti sue itself conta n ng two new essels Hematoxylin and eosin

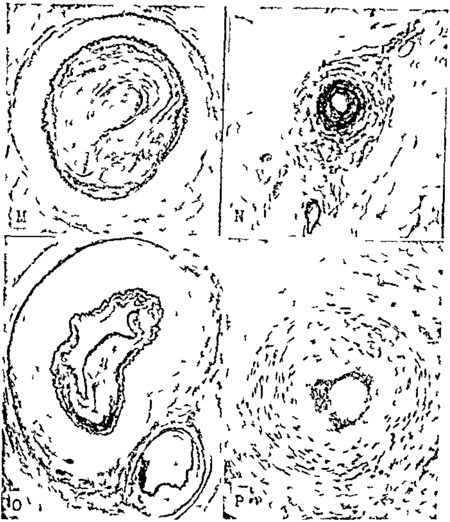


FIG 8 *Cont'd*

(M) Raynaud's phenomenon and scleroderma Digital artery near end of left index finger A thin adventitia surrounds an almost normal media and well defined lamella Lumen blocked by dense fibrous tissue sparsely nucleated containing numerous but fine elastic fibers in outer layers and less or none centrally Center of obstruction consisted of richly cellular tissue Weigert's stain

(N) Tip of fourth left finger one of several arterioles replacing digital artery Adventitia and well defined media and lamella enclosed a very thick intima the latter was full of concentric layers of coarse elastic fibers except for an inner layer directly surrounding the tiny circular lumen Weigert stain

(O) Man of 66 years Warm hands Both digital arteries of this the fourth left finger presented considerable intimal thickening (as exemplified) at some points and moderate thickening at others The figure illustrates the highest grade of obstruction that has been found associated with visible capillary pulsation of the corresponding fingertip

(P) Digital artery at base of right third finger A heavy media Moderately hyperplastic intima Cavity plugged by recent clot with dark staining leukocyte

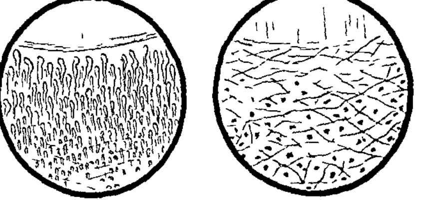


Fig 9—Drawing of the microscopic appearance of the capillary bed at the base of the nail in normal finger (left) and in frost bitten finger (right) Note the hairpin appearance of the normal parallel capillary loops which are absent in the affected finger The thrombosed stumps of the arterioles are characteristic of the frost bitten finger (Davis Scarff Rogers and Dickson[11] courtesy Surg Gynec & Obst)

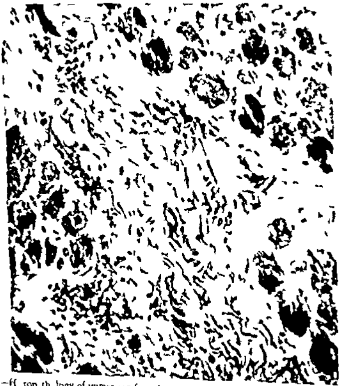


Fig —Histopathology of immersion foot showing necrosis and repair of muscle tissue (White and Warren c u t y War Med n)

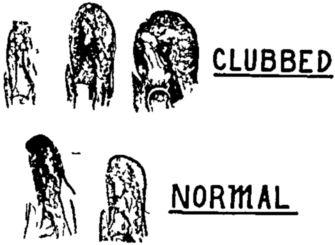
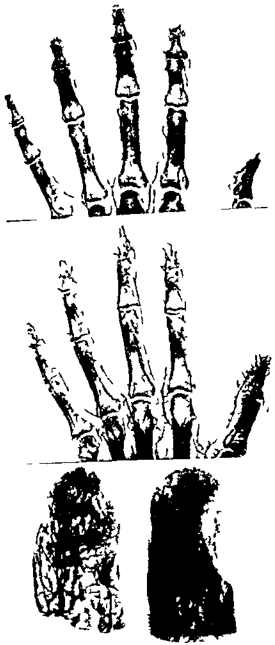


FIG 11 —Photographs of midsagittal sections of terminal digits—cleared cut and stained Despite postmortem shrinkage of tissues hypertrophy and hyp rplasia can be clearly demonstrated in the clubbed fingers when compared with the normal (Mendlowitz [401])



F G 12A (top left)—Arteriogram of the no m l h nd

F G 12B middle)—A teriogram of h d w th clubbed fi gers (Fig 12 A a d B from Charr and S n n rt v Am J Roe tgenol)

F G C (b tt m)—Arteri gram of normal (right) compa ed with a cl bbed finger (left) (Mend l w



FIG 12D —(1 top) Untouched photomicrograph (× 40) of a transverse section 200 μ thick through a normal nail bed Note the extensive venous plexuses The normal arterial arrangement is shown by the course of the artery entering low on the left Arising from it are two groups of darkly stained arteriovenous anastomoses

FIG 12D —(2 middle) Untouched photomicrograph (× 40) of transverse section 200 μ thick through nail bed of a clubbed finger associated with bronchiectasis The veins are little wider than those in fig 12D (1) but appear more widely separated by increased interstitial tissue

FIG 12D —(3 bottom) Untouched photomicrograph (× 40) of transverse section 200 μ thick through nail bed of a clubbed finger associated with cyanotic congenital heart disease The veins are widely dilated *A simple type of arteriovenous anastomosis joins the artery and vein running parallel towards* the surface in the right of the picture (All three illustrations from Lovell[145] courtesy Clinical Science)



F G 13A (top)—A glom ngiom compared with the norm l glomus

F G 13B (bott m)—Microscop c deta l of the structure of the tumor The essels ha e a very narro l m n h ir w lls a e ndist nct a d me g with masses of epithel oid cells m xed with numerou nerve fibe (B th figu e from M s on nd Gery r co rtesy Ann d Anat Path)

METHODS

CAPILLAROSCOPY

Capillaroscopy is usually accomplished by shaving superficial skin from the cuticle of a nail without producing bleeding, placing a drop of oil on the area and observing the capillaries with a dissecting microscope.[135, 630] Capillaries are visualized as loops extending from the arteriolar to the venular side (fig. 14).[336] This loop formation is exaggerated in the nail bed because of the local anatomy of the eponychium, which is a very thin fold of epidermis. The capillary wall can be visualized by injecting dye into the tissues.[51]

It happens that one of the worst places for studying capillaries for purposes of comparison between individuals and for the study of generalized disease is the eponychium.[401] The reason for this is the prevalence of a variety of local changes in this region. Capillary changes, for example, are produced by pushing the cuticle back habitually, by hang nails and by acute or chronic paronychia, as well as by the application of nail polish or other chemicals or simply by washing or scrubbing the hands with soap.





Fig. 14A (top left).—Nail fold capillaries of a young adult. The arterial and venous segments of the hairpin-like loops are equal in caliber. The distal row contains thirteen loops, while twenty-seven crests are visible in the field. The blood flow is uniform and rapid.

Fig. 14B (top right).—Nail fold capillaries of a person of middle age. Although the loops may be long and straight, the number of tortuous loops is usually increased. The apparent difference in the arterial and venous segments may be noted. The flow may be only slightly slow in such loops.



Fig 14C (middle left) —Nail fold capillaries of an old person The number of loops is less and the difference in caliber of the arterial and venous segments is greater than among younger persons The flow is definitely slow in these loops

Fig 14D (middle right) —Nail fold capillaries during syncope or white stage of reaction to moderate cold in a case of Raynaud disease The loops are small capillaries are contracted and partially filled Many loops are still unfilled and thus invisible No movement of blood is seen

Fig 14E (bottom left) —Asphyxia or blue stage of the reaction to moderate cold in Raynaud s disease seen in same field and same case as in fig 14D The loops are increased in number and are markedly dilated There is complete stasis of capillary stream with cyanosis of the blood

Fig 14F (bottom right) — Rubor or red stage of the reaction to moderate cold in Raynaud s disease in same field and case as in figs 14D and 14E The capillary flow is resumed suddenly and the blood changes to bright red The loops gradually decrease in width and many additional loops are visible Plasma spaces result from alternating stasis and flow (Figs 14A F from Roth [409] courtesy W B Saunders Co)

In addition the patency or degree of closure of arteriovenous anastomoses will of course affect the appearance and rate of flow in the capillaries in a very variable manner [401] Since most capillaroscopic studies have been done under unstandardized conditions as far as sympathetic nerve discharge is concerned doubt must be cast on their validity [391] Nevertheless capillaroscopic changes have been described in a variety of diseases [69 226 229 351 489] and some of these changes are consistent Illustra

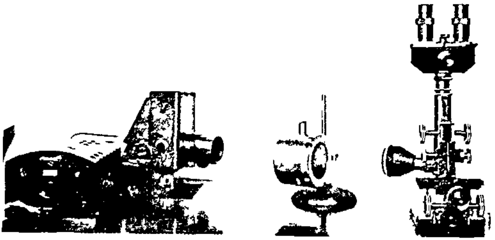


Fig 14G —A photograph of the capillarosocope The Ultropak is attached to the tube of the binocular microscope and is adapted to receive the rays from the carbon arc which is located in a well on the left side of the table A water filter containing a green dye is located between the two The rachet and pinion arrangement at the base of the microscope will move the tube of the scope either forward and backward or from side to side (Duryee and Wright [135] courtesy Am J M Sc)

tions of capillaroscopic findings[489] in various clinical conditions are presented in figure 14

BLOOD PRESSURE

The measurement of digital blood pressure[487] began within a few years of the development of the Riva Rocci Korotkow[303] method for measuring brachial blood pressure Gaertner in 1899 [180] invented a capsule (fig 15) which could be inflated to any desired level of pressure as indicated by a manometer If the finger were blanched with a rubber band prior to such inflation and the rubber band then severed flushing appeared in the fingertip as the pressure was lowered to a level permitting blood to get through The method was superseded by the arm cuff first because pressure is more variable in the finger than in the arm and also because Gaertner did not describe any method for measuring diastolic pressure with his capsule There have been several modifications of the Gaertner capsule each of which is purported to be more convenient or accurate[105, 16, 415] actually there is little difference among them [401] The cuff[596] avoids the necessity of having rings of different sizes since it is essential when using rings to have a snug but not obstructively tight fit [401] The cuff method (figs 16 and 17) or set of rings give values which are about the same [401] Repair of a cuff is difficult whereas the rubber in metal rings is easily replaced after a leak or a tear develops [401]

In 1938 Mendlowitz[389] suggested that the Gaertner capsule could be used to measure diastolic as well as systolic pressure provided studies were carried out after release of sympathetic vasomotor tone by indirect

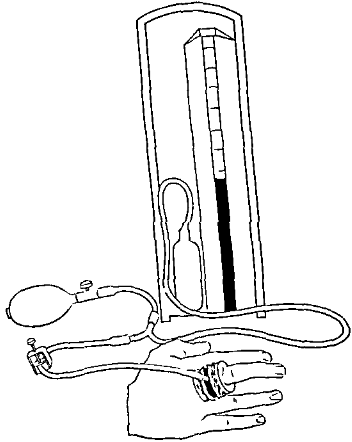


FIG 15A —The Gaertner capsule (Mendlowitz)

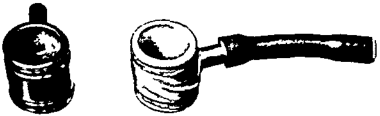


FIG 5B —The Gaertner caps l Th ee ng sizes are u ed for the finger Penrose tubing fixed by rubber b nd l ne the ing (Mendl witz)

heating What is more both systolic and diastolic pressures were more con sistent and less variable under those conditions An old method (von Recklinghausen[592]) for measuring diastolic blood pressure in the arm con sists of the patient s noting the point of cessation of throbbing This checks

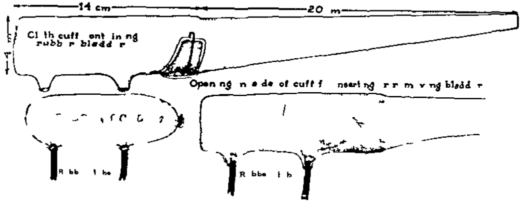


FIG 16 —Digital blood pressure cuff (Weaver and Bohr [596] courtesy Am Heart J)

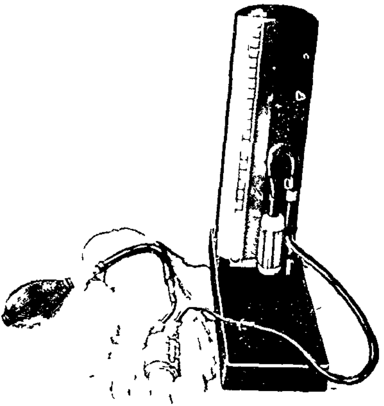


FIG 17 —Digital cuff in place Dorsal view shown to demonstrate connection with manometer when determination of digital pressure are made the hand is supinated (Weaver and Bohr [596] courtesy Am Heart J)

with the auscultatory method which is more objective The same method may be applied to the finger Despite its subjectivity this technic is reliable with a little experience The diastolic level must be checked several times and is the same whether or not there has been prior blanching of the finger with a rubber band cut after the pressure in the cuff is raised

above the systolic level [401] It should be emphasized that the diastolic pressure is variable and inconsistent unless sympathetic nerve discharge is inhibited [401]

The recording oscillometer[337] can measure systolic pressure by the double cuff technic This consists of determining the point of appearance of pulsation in the distal cuff as the pressure in the proximal cuff is lowered Diastolic pressure can also be measured as the pressure in the proximal cuff is lowered to the point where an oblique instead of vertical upswing just prior to the major systolic pulse is seen [337] Digital systolic and diastolic pressure can also be measured by auscultatory amplification (fig 18) [13]

In the toe the systolic blood pressure can usually be measured successfully with the flushing technic but estimation of diastolic pressure is often unsatisfactory even if sympathetic nerve discharge is inhibited [337] [40] The *oscillometric* and auscultatory methods for measuring digital blood pressure are also less satisfactory in the toe than in the finger [337] [10]

True mean pressure can only be determined by planimetric integration of an intra arterial pressure curve [604] The deviation of arithmetic from true mean pressure in the finger is usually *not very great* [399] however

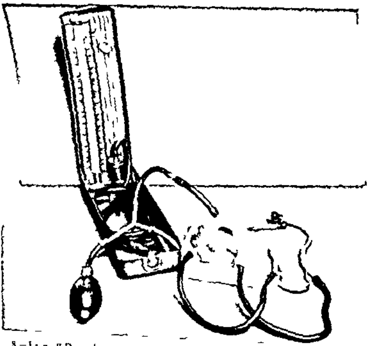


Fig 18—Large B D stethoscope with metal diaphragm and Fox local cuffs for measuring digital [illegible] blood pressure by the auscultatory method If there is discrepancy in pressure between the two [illegible] be detected by a shifting of the sounds from one ear to the other Diastolic [illegible] disappearance of the sensation of pulsation Eurman and Mendlow [illegible]

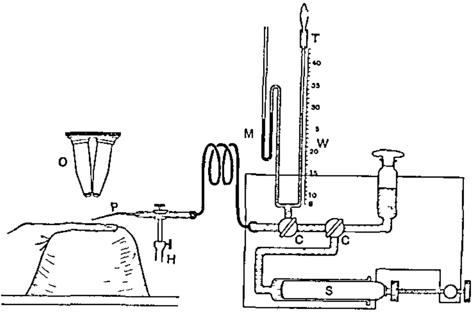


FIG 19 —Diagram of apparatus for the determination of capillary pressure by microinjection (Landis[3 6] courtesy Clinical Science)

Legend P = base of micropipet H = Chambers micromanipulator W = tube T = rubber tubing M = mercury column c c = 3 way stopcocks S = syringe O = Zeiss Greenough binocular microscope (objective 6 orthoscopic oculars f 20 mm) magnification 75

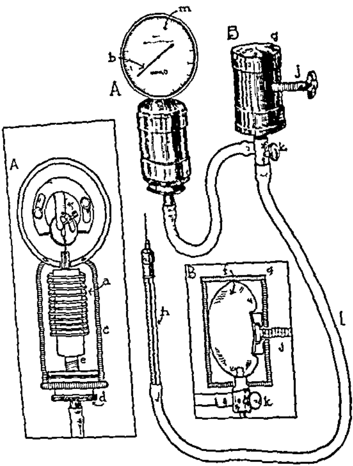
and the former can be interchanged with the latter with little error except in the presence of such conditions for example as aortic insufficiency which produces marked alterations in the form of the pressure curve The normal values for systolic diastolic and arithmetic mean digital arterial pressure as well as brachial digital pressure gradients are presented on page 10

Capillary pressure has been measured in the digit by the insertion of fine glass tubing into the arterial or venous limb of the capillary loop as seen in the eponychium with a capillary microscope (fig 19)[97 326 3 9] Indirect methods[1 4 496] are less reliable[143 145] Carrier and Rehberg[97] found normal capillary pressure (probably of the venous limb of the loop) to be about 5 mm Hg provided the finger were above the level of the clavicle Landis[3 6 3 9] found normal pressure on the arterial side to vary from 21 to 48 and on the venous side of the loop from 6 to 18 mm Hg Venous pressure as measured by the Burch and Winsor phlebomanometer[83] which permits the use of small needles (fig 20) is somewhat higher in the digital veins than it is in the more central veins such as the antecubital (p 10)[441]

BLOOD FLOW AND PULSE WAVES

Skin Temperature

The temperature of the skin of the fingers and toes is more variable than that of any other region of the body This temperature is governed



F G 20—Di gram of the phlebomanometer (B rch and Winsor [illegible] courtesy J A M A)

Legend a = br ss bellows b = needle c = housing d = lock n t e = bellows s pport A = bel low glass le ers bearing a d n edle A = inset for A B = rubber pressure bulb B = inset for B f = pres re bulb g = metal housing h = adapter j = screw-clamp k = alve l = rubber tubing m = d al

by two major factors as in other thermal equilibria [128] The first factor is the heat gained by the finger or toe and the second is the heat lost [122, 484]

Heat may be gained by a finger or toe from two major sources the blood and contact with an object or medium warmer than the part It is chiefly warm arterial blood which contributes heat to the finger [180] Eventually warmed venous blood may also contribute heat both directly and at times indirectly by warming arterial blood previously cooled by adjacent cold venous blood in the venae comites [35, 33] Other sources of intrinsic heat are tissue metabolism and the heat of friction produced by blood moving in blood vessels [397] Under ordinary circumstances both these factors represent a minute fraction of the total heat exchanged in the fingertip or toe (p 67) [397] If the skin is warmed by contact with

a warmer external environment heat will be added to it from this source [130] The efficiency of the heat transfer will depend on the effectiveness of contact specific heat of the environmental substance insulation, and many other factors [46, 609, 610] In general liquids, such as water, are the most efficient media for heat transfer Under ordinary conditions however, nearly all the heat of the fingers or toes is contributed by the arterial blood,[346, 484] and arterial occlusion causes digital temperature to approach the temperature of the ambient medium

Heat is lost from the fingers and toes by the tissues themselves by radiation and by conduction and convection exchanges with the surrounding medium The rate and extent of this loss depends on the difference in temperature between the surrounding atmosphere or medium and the skin [48, 610] Several features of this exchange of heat should be emphasized Factors, such as conductivity area, and thickness of skin may influence the rate of heat exchange [133, 513] Specific heat or heat capacity of the two substances exchanging heat must be known before caloric exchange can be evaluated quantitatively [397] Since determination of heat capacity involves gravimetric measurement, knowledge of the specific gravity or density factor especially of gases, is also necessary in any calculation of heat exchange [396, 397] Generally liquids are much more effective heat acceptors or donors than gases Another factor is the degree of contact between the skin and the recipient substance [401] Liquids are again more effective than gases or solids and the character of surfaces surface tension and wetability become significant [401] Whether the surrounding medium be gas or liquid the factor of jacketing or insulation must always be considered [48, 610] Unless the medium in which the digit is placed circulates rapidly a jacket of gas or liquid is formed the temperature of which is closer to the temperature of the digit than to that of the surrounding medium [553, 554] It is upon such jacketing that the insulating properties of clothing depend [48]

Another important factor in heat loss is the evaporation of skin water or sweat [133] It has been calculated that the evaporation of one gram of water requires 580 calories at 33 C [48, 543, 610] This heat is contributed by the skin as sweat evaporates and is an efficient mechanism for accelerating heat loss Evaporative heat loss is influenced by the skin temperature and by the temperature movement and humidity of the surrounding air [48, 543, 610] *The relationship of skin temperature to various physiologic and pathologic states is represented in table 5* [401]

The reaction of skin temperature to indirect heating[355, 357] is indicated in figure 21 It can be seen that only in the physiologic range is skin temperature parallel to blood flow Above 37 C there is no longer such a relationship since the greater the blood flow the greater the skin heat

TABLE 5.—*Physiologic and Pathologic Reactions which Occur at Various Levels of Skin Temperature* (Modified ...)

Skin Temperature	
	Burns
45 C	
	Reactive Hyperemia Sweating
37 C	
35 C	Regulation of blood flow by patency of arteriovenous anastomoses under sympathetic nervous control
15 C	Critical temperature for lowest blood flow (Raynaud's phenomenon becomes manifest herein susceptible subjects)
12 C	Shivering Reactive hyperemia Trench foot
0 C	Super cooling Ice crystals Frost bite Gangrene
−10 C	

lost rather than gained [180] At 12 to 15 C the lowest blood flow is observed since the factor of reactive hyperemia is not yet active [17] It is in this zone that Raynaud's phenomenon appears [17] An objective test for Raynaud's disease consists of immersing the hands in water at 12 to 15 C for 15 minutes to observe the presence or absence of blanching of the immersed fingers

Reactive hyperemia appears characteristically above 37 C and below 12 C and is due to the release of chemical substances from the cells because of thermal trauma [343, 349] This produces capillary dilatation from a teleologic standpoint serving to wash away these metabolites Sweating and shivering also appear in the upper and lower of these zones respectively although they are influenced more by temperatures of the skin of the trunk than by that of the fingers [48, 343, 410] They are moderator mechanisms tending to keep body and skin temperature within the physiologic or comfort range Above 45 C thermal injury to the skin, if prolonged may become irreversible Such irreversible damage may also be produced by thermal trauma below 12 C At 0 to −10 C ice crystals form in the tissues as a manifestation of frost bite [349] Skin however may be supercooled to as low as −10 C for short periods of time without

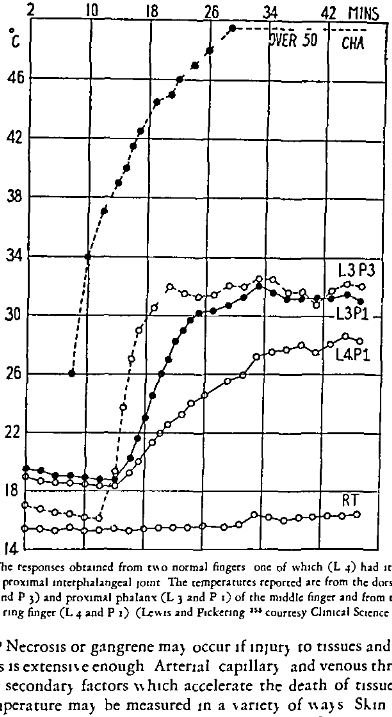


FIG 21 —The responses obtained from two normal fingers one of which (L 4) had its circulation arrested at the proximal interphalangeal joint The temperatures reported are from the dorsum of distal phalanx (L 3 and P 3) and proximal phalanx (L 3 and P 1) of the middle finger and from the proximal phalanx of the ring finger (L 4 and P 1) (Lewis and Pickering [355] courtesy Clinical Science)

freezing [349] Necrosis or gangrene may occur if injury to tissues and destruction of cells is extensive enough Arterial capillary and venous thromboses are usually secondary factors which accelerate the death of tissue [175] [312]

Skin temperature may be measured in a variety of ways Skin mercury thermometers [181] *in use formerly are not very satisfactory because of* their long lag The most widely used device for measuring skin temperature is the thermocouple [484] The principle of the thermocouple[90] [514] is illustrated in figure 22 The point of reference may either be a cold junction or a standard cell Typical circuits[90] for recording with thermocouples,[340] thermopiles [340] resistance thermometers [340] [499] thermisters [74] and radiometers [4] [340] are illustrated in figure 23 The advantages and

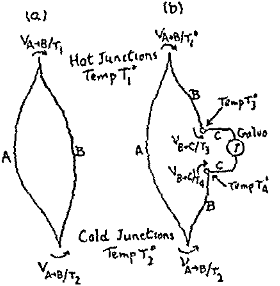


FIG 22 —The principle of the thermocouple T indicates temperature at various points of the circuit whereas V is the voltage (Burton[8] courtesy The Yearbook Publishers Inc)

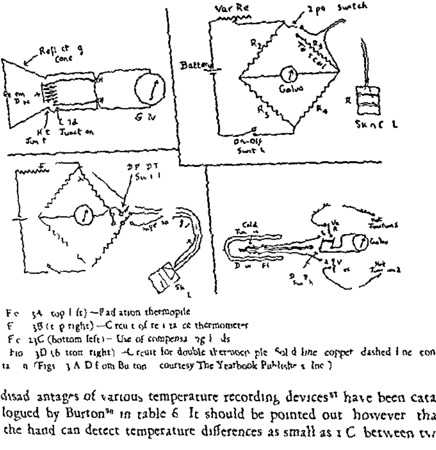


FIG 23A top left (t) —Radiation thermopile
FIG 23B (top right) —Circuit of resistance thermometer
FIG 23C (bottom left) — Use of compensating leads
FIG 23D (bottom right) —Circuit for double thermocouple Solid line copper dashed line constantan (Figs 23 A D from Burton courtesy The Yearbook Publishers Inc)

disadvantages of various temperature recording devices[87] have been catalogued by Burton[30] in table 6 It should be pointed out however that the hand can detect temperature differences as small as 1 C between two

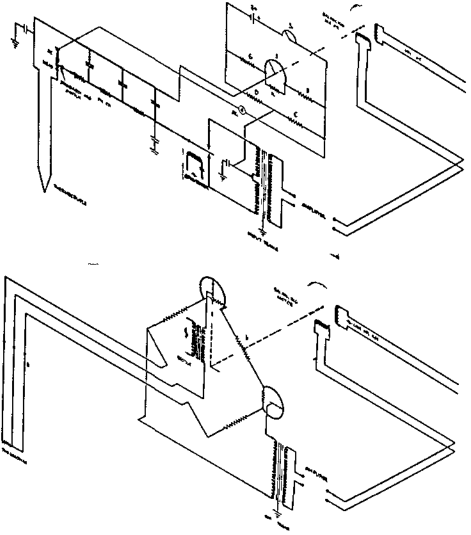


Fig. 23E.—The schematic drawing at the top shows the Speedomax potentiometer circuit for measuring temperature with thermocouples. Any unbalance between thermocouple emf and potentiometer output results in current flow through the filter to the converter input transformer and amplifier. The unbalance signal, converted from d-c to a-c and amplified, is applied to the control winding of the two-phase balancing motor to reposition the slidewire contact and rebalance the circuit.

The drawing at the bottom shows the Speedomax A-C Wheatstone bridge circuit for measuring temperature with Thermohms. The slidewires are synchronized to maintain the resistance of branch a equal to branch b when the resistance of branch r is varied to match the Thermohm and maintain balance. With bridge voltage supplied as indicated, any resistance change in the Thermohm will result in a signal voltage being applied through the input transformer and amplifier to the control winding of the balancing motor to reposition the slidewires and rebalance the circuit. (Both schematics courtesy of Leeds & Northrup.[210])

TABLE 6.—Comparative Evaluation of Electrical Methods for Measuring Skin Temperature (Burt n[66])

	Thermocouples	Thermopiles	Resistance Thermometers
1 Ease of construction	Easy	Difficult	Fairly easy
2 Cost of construction	Low	Higher	Low
3 Sensitivity	Limited by thermoelectric power of metals	Less	Not limited by thermoelectric power
4 Instrumental lag	Can be made very low	Slow unless vacuum thermopiles	Greater than thermocouples
5 Galvanometer required	Moderately sensitive fairly portable	Quite sensitive	Relatively insensitive rugged and portable
6 Possibility of electronic amplification	Not practical	Not easy	Easy
Errors likely	Parasitic Emf s sometimes troublesome change in resistance of leads with temp	Rise of cold junction temp	Heat in coils due to current leads can be automatically compensated
8 Calibration curve	Closely linear in working range	Not linear calculation required	Closely linear
9 Ease of measurement	Cold junction temp must be read	Room temp must be read	No observations except direct scale reading
10 Breakage	Fairly common with fine junctions thermometers break	Not common thermometers break	Fairly common thermometers to break
11 Interference with skin temp	Possible if not properly made	None no contact	Possible if current too high
12 Range of application	Good	Not under clothing	Good
13 Size of area measured	Can be very small hard to average over large area	Area not less than 1 sq cm	Area not less than 0 5 sq cm gives average of large areas
14 Other possible applications	Differential thermocouple for special purposes	Not developed but possible	Differential temp measurement thermal stromuhrs (thermistors)

extremities in a given subject[4 5] Despite the clinical importance of such observations actual temperature estimation is likely to be faulty since it is conditioned by the temperature of the observer s hand[444]

Skin temperature measurement is of limited clinical value although useful as a research tool It is an indirect and not quantitative measure of blood flow and even in the comfort zone the relationship between skin temperature and blood flow is probably not linear[401] Because of lag moreover rapid changes in flow including phasic or systolic diastolic variations cannot be measured Comparative measurements in different individuals[77 4 5 415 416] are difficult to interpret The Gibbon Landis

test [184] however which is based on the observations of Lewis and Pickering,[355] is helpful in distinguishing vasospastic from structural vascular obstruction, although it is not always definitive in borderline cases This test consists of measuring the skin temperature response of the ten digits of the upper extremities, as well as those of the lower extremities to indirect heating In such tests [4 5] if comparisons are to be made between individuals,[42] *it is desirable to know the basal metabolism*[371 517] *and* to maintain comparable environmental temperature and humidity although the latter factor is of far less importance than the temperature [491 618] Winsor[624 625] uses the skin temperature and plethysmographic responses to heat or to reactive hyperemia as tests for arterial insufficiency Such measurements are useful in such vascular diseases as Raynaud s disease and thromboangiitis obliterans or after sympathetic block or sympathectomy [4 2 484]

Comparative measurements of the temperature of contralateral or ipsilateral fingers are feasible thermoelectrically and the results are valid *provided the same room temperature and humidity is maintained as the* readings are being made

Weighted skin temperature has been used as a measurement of over all skin blood flow [43 556 560] The validity of such calculations has recently been challenged[457] because arterial blood temperature at least in the periphery, is often lower than it is assumed to be from measurement of rectal temperature [38 39] Since these skin temperature measurements involve the skin as a whole rather than the fingertips an analysis of this technic is not germane to this monograph

Measurement of blood flow from skin rectal and atmospheric temperature data has been proposed by Burton[89 91] and recently adapted by Green Perkins and Abernethy [98] to the study of peripheral vascular diseases The factors used involve Stewart s principle[553 554] but are applied somewhat differently Blood flow is derived as follows

$$H = C\,(T - T)$$

in which H = heat flow in calories/sq cm /second
T = rectal temperature
T = skin temperature
and C = parameter
Also $H = C(T - T)$
in which C = another parameter
and T = environmental temperature
Since *H* = *H* in the steady state

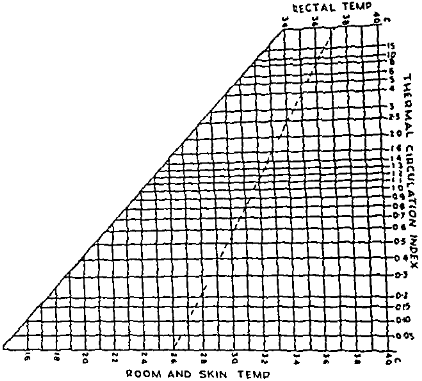
$$C\,(T - T) = C(T - T)$$

thus

$$\frac{C}{C} = \frac{T - T}{T - T} = r$$

in which r is a thermal circulation index

A nomogram of this index at variable skin rectal and room tempera

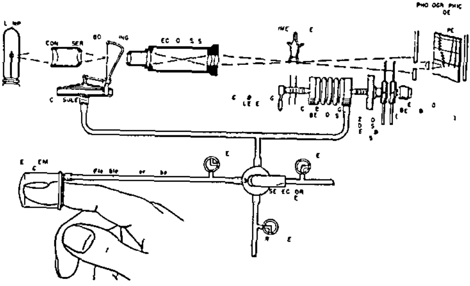


Fi 24 —N m gram for calculation of Thermal Circ lati n Index A thread or layer is laid r the h rt to j n rectal (left side w th r om temperature (right s de) The horizontal line cor r p nd g o k n temperatu e is followed ntil t intercepts th d ag nal The vertical line nearest the p nt f inter t n gi e th thermal ci c lation index (B rton c urtesy The Yearb k Publi hers I c

tures is presented in figure 24 It is to be noted that this index bears only an indirect relationship to blood flow and that this relationship would be modified by sweating[617] and air movement among other factors When Green and his co workers [98] use additional assumptions to convert the data into blood flow values these values are much lower than those obtained by more established methods [297] [614] They therefore represent only relative rather than absolute blood flow One of the reasons for this is the treatment of digital skin as a sample of total epidermis without considering the special functions of the arteriovenous anastomoses [401] Another inherent source of error[23] [25] is the assumption that rectal temperature is equivalent to that of the arterial blood (p 69) Despite these shortcomings this index may be of value in distinguishing normal from grossly abnormal circulation in the digits

Plethysmograph

The digital plethysmograph measures changes in the volume of the fingertip or toe There are several types of such instruments [290] [495] One



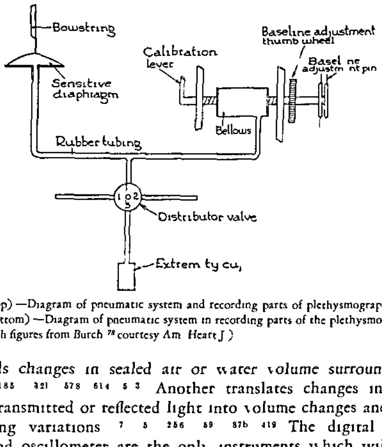


FIG 25A (top) —Diagram of pneumatic system and recording parts of plethysmograph

FIG 25B (bottom) —Diagram of pneumatic system in recording parts of the plethysmograph shown in fig 25A (Both figures from Burch[78] courtesy Am Heart J)

type records changes in sealed air or water volume surrounding the part[77, 78, 185, 321, 578, 614, 583] Another translates changes in the intensity of transmitted or reflected light into volume changes and records corresponding variations[7, 5, 256, 59, 87b, 419] The digital plethysmograph and oscillometer are the only instruments which will record pulsatile changes in the vessels of the fingertip or toe Figures 25 and 26 illustrate the two types of digital plethysmograph Changes in volume of the fingertip as recorded by the digital plethysmograph[60] are attributable to changes in arteriolar tone but may also reflect venous obstruction

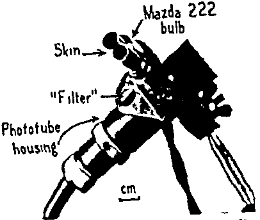


Fig 16 —Photoelectric plethysmograph (Hertzman[88] courtesy The Yearbook Publishers Inc)

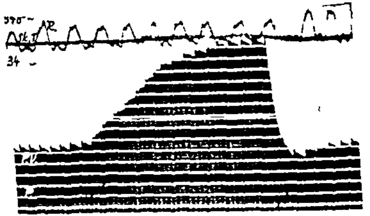


Fig 2 —Typical tracing of venous congestion test second left toe fully dilated Note the initial rise and return to initial level with release of pressure (Goetz[197] courtesy Am Heart J)

or congestion What is more it is conceivable that the velocity of flow might increase through the fingertip or toe without necessarily increasing the volume[101] The volume pulse amplitude on the other hand is a fair index of changes in blood flow[88, 255, 258] although the relationship is not very exact[102] and may be in error in the presence of such conditions as for example aortic insufficiency The form of the pulse wave gives information similar to that obtained by the radial pulse wave recorder[810] piezoelectric sphygmograph[197] continuous arterial pressure wave recorder[810] and recording oscillometer[227] The third derivative of the wave resembles the contours of the ballistocardiogram[82, 447] In the presence of vasoconstriction changes in the dicrotic notch[129] or in the form of the wave are modified more in the digit than at the wrist[252] In hypertension there is a delay in the propagation of the wave from wrist to finger[139] In aortic insufficiency[291] systemic arteriovenous anastomosis or patent

ductus arteriosus [386] the dicrotic notch moves downward on the descending limb of the pulse wave *In coarctation of the aorta the pulsations in the lower extremities are less than in the upper and are of a saw tooth character* [386]

The slope of increasing volume with venous obstruction[65] [64] has been used to measure volume flow in the fingertip (fig 27) [18] Venous obstruction is usually effected by a pressure cuff at the wrist or ankle or by a Gaertner capsule [185] Although in a general way this affords an index of volume flow it is subject to several important sources of error [10] [115] [54] [381] *For example changes in digital blood flow can be measured calorimetrically* after arterial and venous obstruction [403] [413] Typical experiments are presented graphically in figures 28 and 29 The results in many experiments on upper as well as lower extremities (tables 7 and 8) confirm these findings [413] It will be seen that venous obstruction for several minutes decreases blood flow *only slightly, and sometimes not at all* whereas arterial obstruction reduces blood flow in the fingertip or toe sharply, although not quite to the zero level [413]

Experiments in which venous and arterial obstruction are employed for only 30 seconds or less also reveal less decrease in flow during venous than during arterial obstruction although the differences are less striking [413] The lag factor of the digital calorimeter, however, is approximately one minute and each of the series of flow determinations made in any subject covers *a period of one minute* [413] *It would therefore be expected* that such differences as occur with obstruction over a fraction of a minute would be damped to some extent The lower venous pressure in the initial phase of venous obstruction might also be a damping factor (tables 7 and 8) [413]

It is apparent from such experiments that prolonged venous obstruction is incomplete because of considerable reflux of blood probably via deep veins [413] This reflux may occasionally be great enough to accommodate the total influx from the arteries [413] Even with 30 seconds of venous obstruction all the blood is not trapped in the finger or toe [413] There is no evidence bearing on the first 5 or 10 seconds of venous obstruction where *digital plethysmographic slopes are usually drawn The calorimetric* lag is too great to make successful comparisons of flow at such short intervals [413] It must be pointed out however that reflux of blood may occur even during this initial phase of obstruction and may produce a variable error in the measurement of blood flow [413] It has also been demonstrated that at high rates of flow increased pulse volume makes it more difficult to draw accurate digital plethysmographic slopes [385] In contrast, it is at such high rates of flow that the digital calorimeter becomes most reliable [413] In addition to these factors it is clear that

TABLE 4.—*The Effect of Arterial Obstruction on Digital Blood Flow (Mendlowitz, Touroff and Abel*[12]*)*

Digit	Time of obstruction (min)	Flow before obstruction (cc/100 cm min)	Lowest flow during obstruction (cc/100 cm min)	Flow after obstruction (cc/100 cm min)	Maximum percentage change in flow
Great toe	9	0 15	0 01	0 16	−93
	6	0 18	0 01	0 15	−89
	5	0 16	0 02	0 14	−88
	3	0 17	0 03	0 16	−82
	3	0 18	0 07	0 21	−61
	3	0 17	0 [illegible]	0 17	−88
	3	0 26	0 09	0 25	−65
	3	0 16	0 06	0 20	−63
	3	0 18	0 04	0 20	−78
	3	0 15	0 04	0 15	−73
	3	0 17	0 07	0 12	−59
	2	0 18	0 07	0 23	−61
	2	0 19	0 06	0 17	−68
	1½	0 26	0 21	0 23	−19
	1½	0 23	0 18	0 23	−22
	1½	0 27	0 17	0 25	−3
	1½	0 20	0 14	0 20	−30
	2	0 27	0 20	0 26	−26
	1½	0 7	0 12	0 17	−29
	1½	0 4	0 17	0 27	−29
	2	0 14	0 11	0 15	−21
Finger	8	0 34	0 07	0 28	−9
	3	0 32	0 03	0 32	−91
	3	0 24	0 04	0 25	−83
	3	0 32	0 03	0 28	−91
	3	0 12	0 03	0 11	−75
	3	0 26	04	0 24	−85
	3	0 33	05	0 38	−87
	½	0 31	0 23	0 34	−26
	½	0 21	0 16	0 23	−29
	½	0 29	0 23	0 29	−[illegible]
	½	0 2	0 21	0 30	−22
	½	0 24	0 2	0 24	−[illegible]
	½	0 32	0 22	0 33	−31
	½	0 30	0 22	0 33	−27

reflexes induced psychically[413] (fig 30) or by the very act of venous obstruction[6, 413] (fig 31) may break through the inhibition of sympathetic nerve discharge by heating alone and less commonly by heating together with intravenously administered tetraethylammonium chloride to distort flow measurements dependent on such obstruction It has also been shown that at low temperatures the digital circulation is not sufficiently distensible to accommodate blood trapped by venous obstruction[413] Despite these difficulties the plethysmograph is useful for making comparative studies in an individual patient and for noting the response to a

ductus arteriosus[386] the dicrotic notch moves downward on the descending limb of the pulse wave. In coarctation of the aorta the pulsations in the lower extremities are less than in the upper and are of a saw tooth character.[386]

The slope of increasing volume with venous obstruction[65, 64] has been used to measure volume flow in the fingertip (fig. 27).[187] Venous obstruction *is usually* effected by a pressure cuff at the wrist or ankle or by a Gaertner capsule.[185] Although in a general way this affords an index of volume flow it is subject to several important sources of error.[10, 115, 54, 334] For example, changes in digital blood flow can be measured calorimetrically after arterial and venous obstruction.[403, 413] Typical experiments are presented *graphically in figures 28 and 29. The results in many experiments* on upper as well as lower extremities (tables 7 and 8) confirm these findings.[413] It will be seen that venous obstruction for several minutes decreases blood flow only slightly and sometimes not at all, whereas, arterial obstruction reduces blood flow in the fingertip or toe sharply although not quite to the zero level.[413]

Experiments, in which venous and arterial obstruction are employed for only 30 seconds or less also reveal less decrease in flow during venous *than during arterial obstruction, although the differences are less striking.*[413] The lag factor of the digital calorimeter, however, is approximately one minute and each of the series of flow determinations made in any subject covers a period of one minute.[413] It would therefore be expected that such differences as occur with obstruction over a fraction of a minute would be damped to some extent. The lower venous pressure in the initial phase of obstruction might also be a damping factor (tables 7 and 8).[413]

It is apparent from such experiments that prolonged venous obstruction is incomplete because of considerable reflux of blood probably via deep veins.[413] This reflux may occasionally be great enough to accommodate the total influx from the arteries.[413] Even with 30 seconds of venous obstruction all the blood is not trapped in the finger or toe.[413] There is no evidence bearing on the first 5 or 10 seconds of venous obstruction where digital plethysmographic slopes are usually drawn. The calorimetric lag is too great to make successful comparisons of flow at such short intervals.[413] It must be pointed out however that reflux of blood may occur even during this initial phase of obstruction and may produce a variable error in the measurement of blood flow.[413] It has also been demonstrated *that at high rates of flow increased* pulse volume makes it more difficult to draw accurate digital plethysmographic slopes.[385] In contrast it is at such high rates of flow that the digital calorimeter becomes most reliable.[413] In addition *to these factors it is clear that*

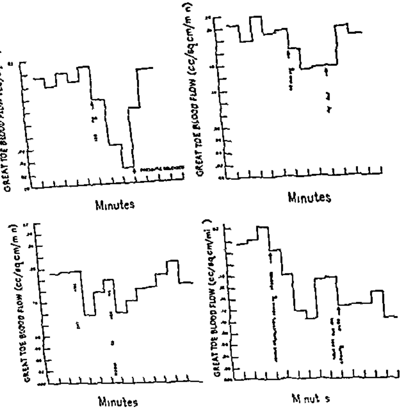


FIG 28 (top left)—The effect of arterial occlusion on digital blood flow (toe)
FIG 29 (top right)—The effect of venous occlusion on digital blood flow (toe)
FIG 30 (bottom left)—The effect of psychic stimuli on digital blood flow (toe)
FIG 31 (bottom right)—Reflex vasoconstriction produced by venous occlusion (Figs 28 30 from Mendlowitz Touroff and Abel courtesy J Clin Investigation)

In figures 32 and 33 plethysmographic records of various types[155, 333] illustrate the effect of drugs[21, 189, 191] the effect of changes in environmental temperature[241, 26, 269, 291, 420] of emotion and of sympathetic nerve block[290] on the digital circulation

Oscillometer

Electronic and recording oscillometers[159, 295, 98, 337, 150, 300] have recently been developed and adapted for studying digital as well as brachial pulse waves A photograph and diagram of such an instrument[337] is presented in figure 34 The increased sensitivity of the instrument often introduces base line artefacts but continuous tracings of major and dicrotic waves can be easily recorded[337] (fig 35) The digital systolic and diastolic pressure can be measured objectively with this instrument within the limitations of all such methods (p 47) Changes in the dicrotic waves

TABLE 8 —*The Effect of Venous Obstruction on Digital Blood Flow (Mendlowitz Touroff and Abel*[113]*)*

Digit	Time of obstruction (min)	Flow before obstruction (cc /sq cm /min)	Lowest flow during obstruction (cc /sq cm /min)	Flow after obstruction (cc /sq cm /min)	Maximum per cent change in flow
Great toe	9	0 23	0 14	0 24	−39
	4	0 21	0 15	0 30	−29
	4	0 08	0 05	0 08	−38
	4	0 17	0 14	0 18	−18
	3	0 15	0 12	0 14	−20
	3	0 05	0 04	0 09	−20
	3	0 17	0 11	0 15	−35
	3	0 23	0 17	0 23	−26
	3	0 15	0 16	0 16	+7
	3	0 25	0 18	0 28	−28
	2	0 23	0 23	0 26	0
	2	0 13	0 08	0 10	−38
	2	0 21	0 18	0 24	−14
	2	0 16	0 13	0 16	−19
	2	0 16	0 13	0 15	−19
	½	0 06	0 06	0 06	0
	½	0 15	0 12	0 16	−20
	½	0 12	0 13	0 13	+8
	½	0 19	0 18	0 18	−5
	½	0 28	0 12	0 30	−57
	½	0 19	0 15	0 19	−21
	½	0 14	0 14	0 13	0
	½	0 11	0 11	0 11	0
	½	0 17	0 17	0 17	0
	½	0 16	0 16	0 18	0
Finger	3	0 28	0 26	0 32	−32
	3	0 41	0 22	0 51	−46
	3	0 16	0 06	0 12	−63
	3	0 20	0 18	0 22	−10
	3	0 38	0 24	0 39	−37
	3	0 15	0 08	0 14	−47
	3	0 23	0 18	0 19	−22
	½	0 30	0 26	0 28	−13
	½	0 24	0 21	0 24	−13
	½	0 35	0 31	0 38	−11
	½	0 42	0 36	0 41	−14
	½	0 16	0 15	0 16	−06
	½	0 26	0 23	0 26	−12
	½	0 28	0 24	0 28	−14
	½	0 39	0 36	0 40	−08
	½	0 25	0 21	0 23	−16
	⅓	0 25	0 22	0 25	−12
	⅓	0 29	0 25	0 29	−14
	¼	0 28	0 22	0 27	−21

variety of physiologic stimuli[79, 80] and drugs [1, 189, 191] Wave like changes in pulse amplitude illustrate[79] (fig 5) the sensitivity of the digital circulation to various cyclic stimuli including respiration



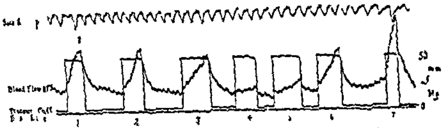


FIG 32D (top)—Blood flow curves from right middle finger (blood flow RF 3) Subject warm and vessels dilated Same experiment as in fig 32E Calculated values in cc per minute per 10 cc finger volume —Curve No 1 5 4 cc No 2 4 3 cc No 3 6 6 cc No 4 5 4 cc No 5 8 0 cc

FIG 32E (bottom)—Blood flow curves from right middle finger (Blood flow RF 3) Subject comfortable neither hot nor cold In respiratory tracing (Resp) down stroke represents inspiration Pressure with a congesting cuff (Pressure cuff) is 10 mm Hg as shown on appended scale These are the same for all records Calculated values in cc per minute per 10 cc finger volume —Curve No 1 1 0 cc No 2 9 cc No 3 0 5 cc No 4 0 8 cc No 5 0 18 cc No 6 0 66 cc No 2 0 cc (Figs 32 D and E from Wilkins Doupe and Newman courtesy Clinical Science)

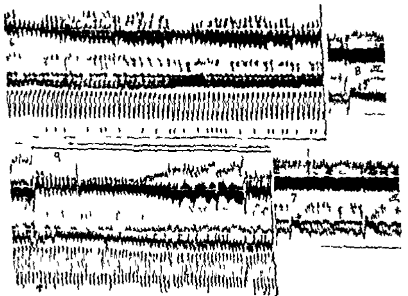


FIG 33 —In Fig 33 6 9 represent volume pulses of finger pads and of digital artery at first interphalangeal joint 6 Spontaneous waves Upper record of pad Respiration and time in 5 seconds 7 Spontaneous waves Lower record of pad 8 Loud noise Lower record of pad 9 Application of cold to finger whose pad pulses and digital artery pulses are being recorded Upper record of pad Respiration and time in 5 seconds (Hertzman courtesy Am J Physiol)

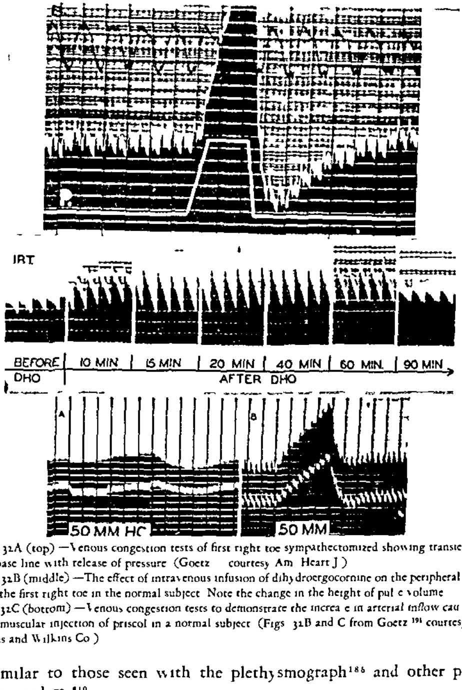


FIG 32A (top) —Venous congestion tests of first right toe sympathectomized showing transient fall below base line with release of pressure (Goetz courtesy Am Heart J)

FIG 32B (middle) —The effect of intravenous infusion of dihydroergocornine on the peripheral blood flow of the first right toe in the normal subject Note the change in the height of pulse volume

FIG 32C (bottom) —Venous congestion tests to demonstrate the increase in arterial *inflow caused by* an intramuscular injection of priscol in a normal subject (Figs 32B and C from Goetz [191] courtesy The Williams and Wilkins Co)

are similar to those seen with the plethysmograph[186] and other pulse wave recorders [810]

Calorimeter

The calorimetric method for measuring blood flow was introduced in 1911 by G N Stewart [661, 654] This method was based on the following principle If the total caloric output of a hand is measured and the arteriovenous temperature difference *is known the amount of blood flowing* through the hand can be computed by dividing the calories by the arterio

venous temperature difference In effect this is a peripheral Fick principle[1] in which heat rather than oxygen exchange is utilized for measuring blood flow A calorimeter was constructed by Stewart[553, 554] to measure the caloric output of the hand The temperature of the arterial blood was assumed to be identical with mouth temperature and if the temperature of the calorimeter were set from 5 to 15 C lower than mouth temperature average calorimeter temperature was considered identical with *venous blood temperature* This implied that all the blood passing through the hand was effectively cooled to the temperature of the calorimeter

In 1927 Harris and Marvin[243] measured the temperature of the *venous* blood at the wrist directly and found that it did not correspond with the calorimeter temperature but could in fact be several centigrade *degrees higher probably* because of uncooled blood from the deeper tissues Stewart s principle[553] was also challenged by Sheard[513] on physical grounds Keggereis in 1926[35] tried to improve the hand calorimetric method by expressing blood flow per unit of surface rather than volume The hand calorimeter was subsequently employed only sporadically[455, 548] Pickering in 1936[460] used it to measure maximum heat elimination in hypertension He considered these values to be proportional to blood flow In 1938 Mendlowitz[389] used the hand calorimeter in the same way in a study of clubbed fingers The apparatus has been modified recently by using flow calorimetry[1, 5, 261] and the adiabatic principle[114, 311] Stewart s principle[5, 3] was also employed in 1938 by Hardy and Soderstrom[243] to measure average skin blood flow quantitatively These workers assumed mouth or rectal temperature to represent that of the arterial blood and average skin temperature to be equal to that of the venous blood They computed blood flow per unit surface area under fixed conditions of room temperature rest and covering but without complete vasodilatation A modification of the same principle was used by Burton[91] and later by Green *et al*[08] to measure fingertip blood flow from skin temperature data (p 52)

In 1938 Mendlowitz[389] constructed a calorimeter to measure the heat output of the fingertip and in 1941[390] this method was found adaptable to the measurement of blood flow rather than heat elimination All measurements were done at heart level[394] after complete vasodilatation by indirect heating Because of its narrow normal range of variation this technic was successfully used to study hemodynamic changes in clubbed fingers[389, 39] hypertension[39, 398, 400] coronary occlusion[39] anemia polycythemia[394, 395] and various peripheral vascular diseases[398, 402, 404, 405] The digital calorimetric method is none the less also indirect and the assumptions involved must be subjected to searching critical analysis

The digital calorimeter (figs 36 and 37) consists of a polished aluminum

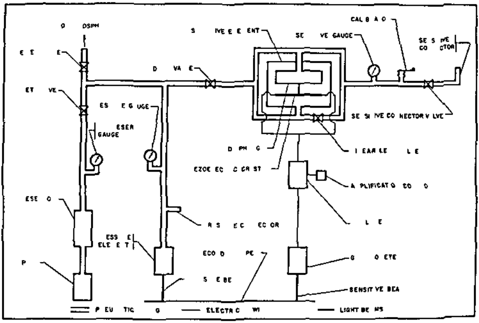


FIG 34 —Diagram of electronic recording oscillometer (Lax and Feinberg [337] Reproduced with authors permission)

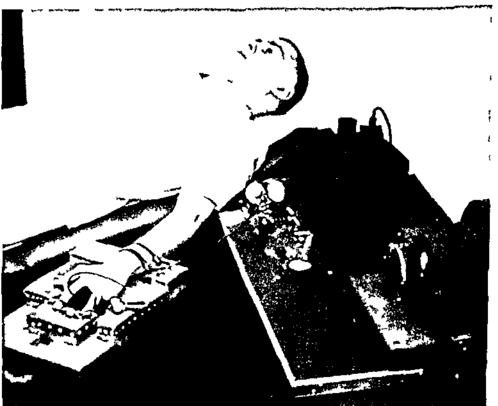


FIG 35 —Recording electronic oscillometer in u e (Lax and Feinberg [33] reproduced with authors permission)

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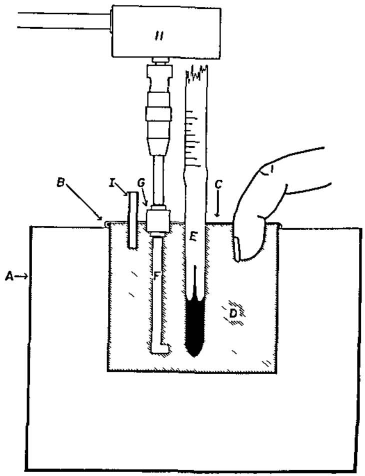


FIG 36 —Calorimeter for the finger (Mendlowitz [389] modified courtesy Clinical Science)

cup filled with water and surrounded by broken cork in a large wooden box [397] The cup is covered tightly by a rubber membrane with apertures for a stirrer Beckmann thermometer air vent and the fingertip or great toe [397] The apertures are designed to prevent leakage of water and to avoid contact between the digit and thermometer stirrer or inner side of the cup [397] The fingertip calorimeter holds approximately 100 cc and the great toe calorimeter 200 cc of water [397] The stirrer may be a glass rod with a horizontal metal loop designed for up and down hand stirring or an electric rotary or electromagnetic stirrer An air vent via a small glass tube has also been found useful to prevent spattering of water around the stirring jacket [397]

Blood flow is usually measured with this calorimeter after vasodilatation by indirect heating [3, 346] This may be achieved by a special electric blanket [397] an electric bulb cradle baker [397] a diathermy apparatus [397] an electrically heated sleeve [71] or a stirred arm water bath maintained at 45 C [346] Maximum vasodilatation in the hand is usually heralded by the onset of sweating and reaches a plateau after from 20 to 30 minutes

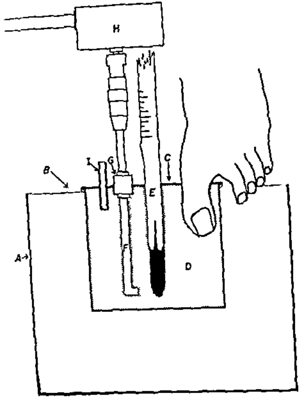


Fig 3 —Calorimeter for the toe A = a wooden box containing broken cork B = a layer of absorbent cotton C = rubber membrane fixed to the lip of the cup by a rubber band D = water in the polished aluminum calorimeter cup the volume of which is 200 cc for the toe and 100 cc for the digital calorimeter E = Beckman thermometer F = glass stirring rod G = rubber covered glass sleeve H = motor (Mendlowitz and Abel[2] courtesy Grune & Stratton)

of heating[346] For the toe 45 to 90 minutes of heating may be required[402] Maximum vasodilatation in the toe may also be achieved by indirect heating for 30 minutes supplemented by the intravenous administration of 300 to 500 mg of tetraethylammonium chloride or 0 8 mg /kg of SC 1950[404] That vasodilatation in the upper extremity is complete after indirect heating was demonstrated by Arnott and Macfie[22] These workers could not after indirect heating increase heat elimination from the fifth fingertip measured calorimetrically by procaine block of the ulnar nerve We have also been unable to demonstrate an increase in blood flow in the skin of the great toe after spinal anesthesia over that produced by indirect heating supplemented by intravenous tetraethylammonium chloride (p 16)[414]

Blood flow is computed from the formula[397]

$$Q = \frac{(\Delta t + \Delta t)(m + e)}{\rho c \ (t - t)}$$

where Q = blood flow in cc /sq cm /minute
Δt_1 = rise in temperature of calorimeter in centigrade degrees per minute with the fingertip or toe inserted
Δt_2 = fall in temperature p r minute in centigrade degrees due to the difference between calorimeter and room temperature a cork replacing the finger tip or toe
m = volume or weight of water in the cup
e = hydrothermic equivalent of the cup thermometer bulb mercury the metal if any of the stirrer and the finger tip or toe
ρ = specific heat of the blood
ϕ = sp cific gravity of th blood
a = surface area of the finger tip or to in sq cm
t_3 = temperature of arterial blood (mouth temp rature minus 0 7 C)
t_4 = temperature of venous blood (average calorimeter temperature)

Analysis of the numerator of this formula indicates that it represents the gram calories per minute elaborated by the fingertip or toe [397] This is computed by multiplying the total rise in temperature per minute ($\Delta t_1 + \Delta t$) by the volume and hence weight of the water in the cup to which is added the water equivalent of both the calorimeter and the fingertip or toe The observed rise in temperature of the calorimeter with the digit inserted Δt_1 is actually the total heat output of the finger minus the fall in temperature, Δt, due to the difference between room and calorimeter temperature The latter is measured by substituting a cork for the fingertip or toe [397]

There are several sources of potential error in this arrangement each of which will be considered in detail Sheard pointed out in 1926[513] that the variable factors of conductivity coefficient and thickness of skin could produce a variable lag in transfer of heat from the tissues to the calorimeter In actual practice, readings are not made until the rise in temperature per minute is fairly constant [397] For the first few minutes the readings are often too high due to the loss of retained heat from the fingertip or toe to the calorimeter [397] When the readings become constant over a period of from 5 to 10 minutes it is clear that the lag at the beginning will be neutralized at the end of the period of observation [397] The rise in temperature over this period of time (5 to 10 minutes) must be relatively small that is 1 C or less [397] It is only when the temperature change is small that the readings are constant If the calorimeter temperature rapidly approached that of the arterial blood the rise in temperature per minute would decrease rapidly and the lag factor might introduce some error [397] The calorimeters for both the toe and fingertip are so designed therefore as to keep the rise in temperature over the period of observation below 1 C and usually less than 0 5 C [397]

The heat of stirring may also be a possible source of error If the rate of stirring is constant it can be demonstrated that the stirring factor is cancelled [397]

If a = heat of stirring
b = temperature rise per minute caused by the digital circulation
and
c = heat lost by the calorimeter per minute due to the difference between calorimeter and room temperature
then

$$\Delta t_1 = a + b$$
$$\Delta t_2 = c - a$$

and hence

$$\Delta t_1 + \Delta t = b + c \text{ the heat of stirring } a \text{ having been cancelled}$$

Conduction of heat from the finger above the immersed segment into the calorimeter is a potential source of error especially if it is variable The temperature differential however is small [78] and heat conducted downward from the tissue above the calorimeter has been calculated and found negligible Variability of conduction and radiation of heat from the calorimeter is minimized by maintaining a relatively constant room temperature and humidity during both phases of the procedure [297]

It is assumed in the formula for measuring blood flow that all the heat elaborated by the fingertip or toe is contributed by the arterial blood [79] This assumption would be *invalid if any significant* amount of heat were added to the blood as it passed through the digit There are two possible sources of such heat metabolism and friction The heat produced by frictional resistance to blood flow can be calculated to be a minute and negligible fraction of the total caloric output of the finger tip [297]

Metabolic heat of a fingertip may be estimated as follows[297] The calorific value of oxygen at a respiratory quotient of 0 82 is 4 825 kg per liter [121] The oxygen consumption of a middle aged 70 kg male 152 cm tall is 238 cc per minute [123] The number of calories elaborated per minute by such a man would therefore be 0 238 times 4825 or 1148 calories The caloric output per Gm of tissue would be 1148/70 000 or about 0 02 calories Since an average fingertip weighs 5 Gm the metabolic heat would be about 0 10 calories whereas the usual caloric output of the fingertip in a blood flow determination is about 25 calories [297] The actual contribution of metabolic heat is probably even less than indicated by these averages since the metabolism of the tissue of a digit is relatively low in comparison with that of muscle or glandular tissue [297] Since the blood flow is usually lower per unit of tissue in the toe than in the fingertip the percentage contribution of metabolism is greater but still insignificant [?] To test these calculations the caloric output of the fingertip and toe were measured with occluding cuffs on the upper arm wrist and finger or on the ankle and toe [297] [413] Multiple cuffs were necessary to insure the absence of collateral flow via the nutrient vessels of the bones [?]

Collateral bone flow could not be completely eliminated if the vessels of the digit were dilated [413]

The weight, m, of the water in the cup is obtained by measuring its volume [397] In the temperature range at which the calorimeter is maintained the specific gravity of water is such that conversion of volume to weight is valid The slight addition to this contributed by sweat is within the experimental error of water volume measurement [397]

The factor, e, may be approximated[397] as the sum of the water equivalents of the calorimeter cup (weight of the cup × the specific heat of aluminum), the thermometer mercury (obtained by multiplying the volume of mercury in the bulb by its specific gravity and then by its specific heat) and the digit (the volume of the digit × 0 8, the product of tissue specific heat and specific gravity) The water equivalent of the glass of the stirrer and thermometer is small enough to be ignored Another minor source of error is introduced by substituting a cork for the digit in the measurement of Δt, the specific heat and gravity of cork being different from that of tissue [397] These errors can be seen to be insignificant from the fact that the total *e for the finger is approximately 10 cc* (volume of water 100 cc) and for the toe approximately 25 cc (volume of water 200 cc) Even a 50 per cent error in e would represent only a 5 percent error in flow [397]

The denominator in the formula for measuring blood flow contains the factors necessary for the conversion of gram calories per minute into volume flow The number of degrees of temperature each gram of blood loses as it passes through the digit is equal to the number of calories delivered to the calorimeter except as modified by the specific heat of blood [397] If therefore the number of calories elaborated per minute is known the number of grams flowing through the fingertip can be calculated by dividing by the arteriovenous temperature difference and the specific heat of blood [396] The flow is now expressed in grams per minute To convert to cubic centimeters per minute further division by the specific gravity of the blood must be made and to convert to cubic centimeters per square centimeter per minute the final flow in cubic centimeters must be divided by the total area of the immersed portion of the digit in square *centimeters* [397]

If the plasma protein concentration is assumed to be normal both specific heat and specific gravity of blood can be calculated from the hematocrit by interpolation from the known specific heat and gravity of plasma and cells [396, 397] Comparison between actual and calculated specific heat is shown in table 9 [396] Only extreme deviations from the normal plasma proteins are sufficient to modify the product of specific heat and gravity significantly [397] The relationship between hematocrit specific heat specific gravity and the product of the latter two is presented in table 10 [397]

Table 9.—Specific Heat of Random Blood Samples Compared with Specific Heat Calculated from Hematocrits (Mendlowitz[396])

Sample no.	1	2	3	4
Hematocrit, volumetric uncorrected	32.4	42.4	41.6	30.0
Specific heat, calculated	0.89	0.8	0.87	0.89
Specific heat, actual	0.89	0.86	0.86	0.88

It should be pointed out that after vasodilatation by indirect heating nearly all the blood flowing through the digit, especially at the tip, traverses the subcutaneous arteriovenous anastomoses or glomera.[1, 397] Capillary blood flow in the fingertip is also chiefly surface flow.[397] The vascularity depth variable, therefore, emphasized by Sheard[515] in criticism of the hand calorimeter does not apply to the fingertip.[397] Both Sheard[515] and Kegerreis[333] also emphasized that heat elimination is a function of surface area rather than volume and this applies to the digit as well as the hand.[397] Blood flow in our studies has therefore always been expressed in terms of the area of the immersed portion of the toe or fingertip.[397] To determine the area of the immersed digit, the level of immersion is marked with ink. Since the number of glomera per square centimeter decreases from the distal to the proximal portion of the digit, it is important in successive blood flow determinations as well as in comparative determinations to fix the level of immersion at the distal crease.[397] After the level is marked, the immersed portion of the digit is covered with rectangular strips of adhesive tape cut to sizes calculated to produce smooth fitting and these are subsequently measured. With experience, error due to imperfect fitting becomes negligible.[397] Although area may be estimated from digital volume,[288] direct measurement is more accurate.[4, illegible]

The temperature of the digital arterial blood as it reaches the fingertip or toe is represented by t_2. The assumption that mouth or rectal temperature is identical with that of arterial blood has recently been challenged by Bazett, Love, Newton, Eisenberg, Day, and Forster.[43] With cooling and consequent vasoconstriction, these workers demonstrated a decrease in arterial blood temperature to as low as 20 C. The effect is produced by cold blood in the venae comites adjacent to the arteries.[43, 188] These observations invalidate any derivation of blood flow from calorimetric data obtained from cold skin. This includes G. N. Stewart's hand calorimeter,[555] Hardy and Soderstrom's method[243] for the determination of total skin blood flow, and its modification by H. G. Stewart and Evans,[556, 560] and also the digital calorimeter.[289, 397] Calorimetric measurement of digital blood flow, however, has always been carried out only after complete inhibition of sympathetic discharge by indirect heat.[397]

TABLE 10—*The Specific Heat Specific Gravity and Their Product as Calculated from Hematocrits (Mendlowitz[397])*

Hematocrit (volumetric)	Specific heat (ρ)	Specific Gravity (ϕ)	Factor ($\rho\phi$)
10	923	1 034	95
11	921	1 034	95
12	918	1 035	95
13	917	1 036	95
14	916	1 037	95
15	914	1 038	95
16	913	1 038	95
17	912	1 039	95
18	911	1 040	95
19	909	1 041	95
20	906	1 042	94
21	904	1 042	94
22	902	1 043	94
23	900	1 044	94
24	899	1 045	94
25	897	1 046	94
26	895	1 046	94
27	893	1 047	94
28	892	1 048	93
29	890	1 048	93
30	889	1 049	93
31	887	1 050	93
32	885	1 051	93
33	884	1 052	93
34	882	1 052	93
35	880	1 053	93
36	878	1 054	92
37	877	1 055	92
38	874	1 056	9-
39	873	1 056	92
40	872	1 057	92
41	871	1 058	92
42	869	1 059	92
43	867	1 060	92
44	865	1 060	92
45	864	1 061	92
46	862	1 062	92
47	861	1 063	91
48	859	1 064	91
49	857	1 065	91
50	855	1 065	91
51	854	1 066	91
52	852	1 067	91
53	851	1 068	91
54	848	1 068	91
55	846	1 069	91
56	845	1 070	90
57	844	1 071	90
58	843	1 071	90
59	841	1 072	90
60	839	1 073	90
61	838	1 0 4	90
62	836	1 075	90
63	835	1 075	90
64	833	1 076	90
65	831	1 077	90
66	830	1 0 8	89
67	828	1 078	89
68	826	1 079	89
69	825	1 080	89
70	824	1 081	89

TABLE 11 — The Difference Between Mouth and Rectal Arterial Blood Temperature After Release of Sympathetic Nerve Tone by Indirect Heating (Mendlowitz)

Patient	Age	Sex	Mouth temperature (C)	Arterial temperature (C)	Mouth-arterial temperature Diff (C)
H G	59	M	37 4	36 8	0 6
D L	35	M	37 1	36 6	0 5
J W	16	M	3 3	36 5	0 8
E W	30	M	37 8	36 8	1 0
L F	36	M	36 9	36 4	0 5
Average			37 3	36 6	0 7

It therefore becomes important to determine whether mouth or rectal temperature and arterial blood temperature can be considered equivalent under these conditions After indirect heating the difference between mouth and rectal temperature becomes smaller and mouth temperature less variable than it is ordinarily [397] Bazett found radial arterial blood temperature after vasodilatation by indirect heating to be about 36 5 C [40] This was confirmed in five observations of arterial blood temperature measured with a needle thermocouple inserted into the radial artery after prior infiltration with procaine [397] These temperatures obtained after indirect heating are compared with mouth temperatures in table 11 [397] On the basis of these results it is recommended that arterial blood temperature t_2 be considered equivalent to mouth temperature *minus* 0 7 C [397] This would have the effect of shifting both normal and abnormal prior readings upward about 11 per cent [397]

An indirect test of the effect of cold venous blood on arterial blood temperature was carried out by measuring blood flow at varying calorimeter temperatures in the same subject the circulation having been stabilized by indirect heating [397] The good correspondence of the results (table 12)

TABLE 12 — The Difference in Blood Flow at Low Compared with High Calorimeter Temperatures (Mendlowitz [397])

Patient	Age	Sex	Diagnosis	Calorimeter temperature (C)	Blood flow (cc/cm²/min)	Calorimeter temperature (C)	Blood flow (cc/cm²/min)	Difference in blood flow
M E	53	F	Hepatitis	20 20	0 20	18 0	0 22	+0 02
O B	43	F	Anemia	25 0	0 20	18 70	0 23	+0 03
D M	24	F	Hepatitis	18 34	0 24	18 70	0 29	+0 05
J S	20	F	Normal	18 34	0 29	18 70	0 25	−0 03
B O	33	F	Choledochodysk esia	20 20	0 23	18 70	0 23	0 00

TABLE 10.—*The Specific Heat, Specific Gravity and Their Product as Calculated from Hematocrits (Mendlowitz[397])*

Hematocrit (volumetric)	Specific heat (ρ)	Specific Gravity (ϕ)	Factor ($\rho\phi$)
10	923	1 034	95
11	921	1 034	95
12	918	1 035	95
13	917	1 036	95
14	916	1 037	95
15	914	1 038	95
16	913	1 038	95
17	912	1 039	95
18	911	1 040	95
19	909	1 041	95
20	906	1 042	94
21	904	1 042	94
22	902	1 043	94
23	900	1 044	94
24	899	1 045	94
25	897	1 046	94
26	895	1 046	94
27	893	1 047	94
28	892	1 048	93
29	890	1 048	93
30	889	1 049	93
31	887	1 050	93
32	885	1 051	93
33	884	1 052	93
34	882	1 052	93
35	880	1 053	93
36	878	1 054	92
37	877	1 055	92
38	874	1 056	92
39	873	1 056	92
40	872	1 057	92
41	871	1 058	92
42	869	1 059	92
43	867	1 060	92
44	865	1 060	92
45	864	1 061	92
46	862	1 062	91
47	861	1 063	91
48	859	1 064	91
49	857	1 065	91
50	855	1 065	91
51	854	1 066	91
52	852	1 067	91
53	851	1 068	91
54	848	1 068	91
55	846	1 069	90
56	845	1 070	90
57	844	1 071	90
58	843	1 071	90
59	841	1 072	90
60	839	1 073	90
61	838	1 074	90
62	836	1 075	90
63	835	1 075	90
64	833	1 076	90
65	831	1 077	89
66	830	1 078	89
67	828	1 078	89
68	826	1 079	89
69	825	1 080	89
70	824	1 081	

TABLE 13.—*Simultaneous Temperatures of Calorimeter and Digital Venous Blood After Release of Sympathetic Nerve Tone by Indirect Heating in Four Subjects* (Mendlowitz[402])

	Temperature of venous blood (C.)	Temperature of calorimeter (C.)
1	31.8	30.9
2	31.8	31.0
3	31.5	31.0
4	31.6	31.4

presumably from the deeper tissues of the finger. Since the number of arteriovenous anastomoses per unit of tissue increases from the base to the tip of the finger and the ratio of surface area to volume also increases, it was reasoned that if the temperature of venous blood could be measured as it issued from the immersed terminal phalanx, the blood, cooled to the temperature of the calorimeter, would approximate 100 per cent. What is more, blood flow is expressed in terms of surface rather than volume and surface cooling is certainly efficient.[397] The validity of considering average calorimeter temperature equal to that of the venous blood is hence considered reasonably established.[397]

Although the over-all probable error of the procedure cannot be measured exactly, it is undoubtedly small.[397] Repeated measurements in the same subject vary very little and are often identical. The normal range of variation is 0.25 to 0.38 cc./sq. cm./minute for the fingertip and 0.15 to 0.29 cc./sq. cm./minute for the toe.[397, 402, 404] Deviations from the normal are seldom obscured by overlapping because of the narrowness of this normal range. The normal range for the finger has recently been confirmed by Caprighone and Duque.[36] The correct factors for specific heat and specific gravity and the arterial temperature correction make their range almost exactly the same as that of Mendlowitz.[397]

Greenfield et al. have devised an adiabatic digital calorimeter (fig. 39*a*), thus giving the instrument more range for physiologic studies.[212] They were able to demonstrate direct and axone reflex vasodilatation[215, 218, 242] with high blood flow values even when the digit was immersed in very cold water.[10, 212, 13, 217, 218] At low levels of temperature, however, the potential errors of the technic increase and one can only speak of estimated rather than actual blood flow.[403] A recording calorimeter electromagnetically stirred and compensated for heat loss to the atmosphere by a resistance wire was introduced by Mendlowitz (fig. 39*b, c*).[400b] If this calorimeter is given adequate range by a cooling system, the electric current needed to keep the instrument isothermic can be recorded as blood flow.

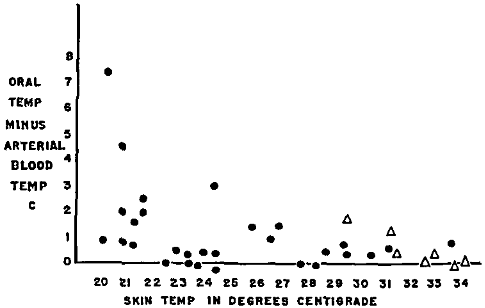


FIG 38 —● = Direct radial arterial blood temperatures subtracted from oral temperatures and plotted against average digital skin temperatures
△ = Indirect digital arterial blood temperatures subtracted from oral temperatures and plotted against average digital skin temperatures
Above a skin temperature of 25 C the average deviation of direct radial arterial blood temperature from oral temperature is −0 6 C and of indirect digital arterial blood temperatures −0 5 C (Eurman and Mendlowitz [160] courtesy J Applied Physiol)

indicates that after release of sympathetic vasomotor tone cooling of digital arterial blood by blood of variable coolness in the digital veins is unimportant as a source of error in this technic [397] It is possible however that at low digital flow levels, the temperature of the arterial blood decreases to a point where the actual flows are higher than represented by calorimetric data [404] If variations in the temperature of arterial blood can be defined by skin temperature measurements more accurate calorimetric flow readings at low rates of flow may be obtained (fig 38) [160]

The temperature of the venous blood t_4 is taken to be identical with the average calorimeter temperature over the period during which heat output is measured [397] This is usually 5 minutes more or less and over a range of from 0 5 to 1 0 C Calorimeter temperature should be kept below 30 C to avoid direct heat vasodilatation [164] In 1942 the validity for the fingertip of Harris and Marvin s [43] criticism of the Stewart method for the hand [553] was tested by measuring venous blood temperature after vasodilatation (table 13) [39] A needle thermocouple was inserted into a vein at the base of a finger immersed completely in a stirred calorimeter It was found that approximately 90 per cent of the blood was cooled to the temperature of the calorimeter the remaining 10 per cent coming

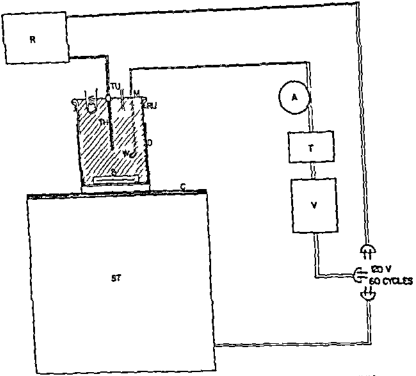


FIG 39B—Diagram of recording digital calorimeter (Mendlowitz [400b])

V = variable voltage control T = step down transformer A = milliammeter R = recorder (Leeds-Northrup #6 452) Tu = glass tube M = rubber membrane Ru = rubber band Th = platinum resistance thermometer (a Beckmann thermometer can be substituted if no record is required) W = resistance wire ensheathed in polyethylene tubing B = plastic stirring bar D = silvered evacuated double walled glass calorimeter cup containing water Cemented to the cup is a metal sheath only the edge of which stands on the cork slab beneath A clamp and ring stand not shown in the diagram hold the unit in place on the stirrer C = cork slab St = electro magnetic stirrer (large)

appearance of a color change in the digit may be measured [455] The degree of functional digital vasoconstriction will introduce great variations in results obtained by this technic [401] It has some application to the determination of relative viability of tissues when the question of amputation is under consideration

The rate of disappearance of radiosodium from tissues is in a sense a semiquantitative measure of the capillary circulatory rate [301, 631] but the correlation is probably marred by anything changing the rate of diffusion from tissues to capillaries other than increase or decrease in blood flow [4] This technic is also useful in estimating viability of tissues but is rarely used in the digits The histamine flare [269, 544, 548] and the saline wheal absorption tests [104, 69, 38, 552] are also rarely used to demonstrate the integrity of digital capillary circulation despite their usefulness in other parts of the extremity

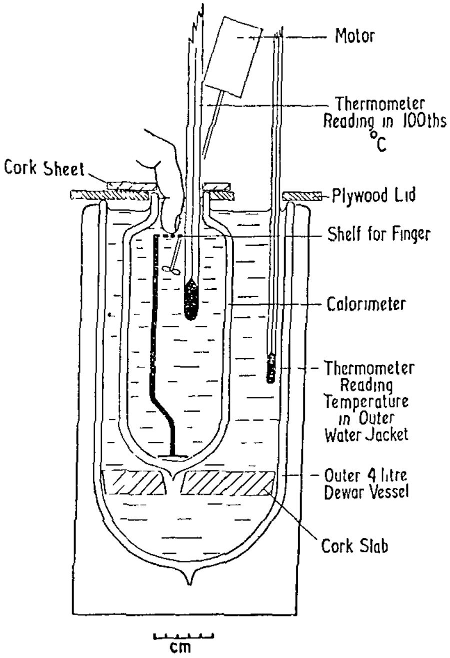


FIG 39 A —Adiabatic digital calorimeter (Greenfield and Shepherd[212] courtesy Clinical Science)

Miscellaneous

There are several other technics for estimating digital circulation some of which are semiquantitative and many of which are better suited to measuring changes in parts of the circulation other than in the digits A radioactive substance or fluorescin for example may be injected into an artery or vein and the time for its appearance in the tissues of the digit may be recorded[30, 33, 51] or the time between breath holding and the

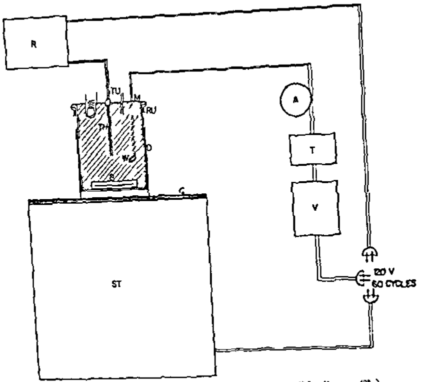


FIG 39B—Diagram of recording digital calorimeter (Mendlowitz[406])
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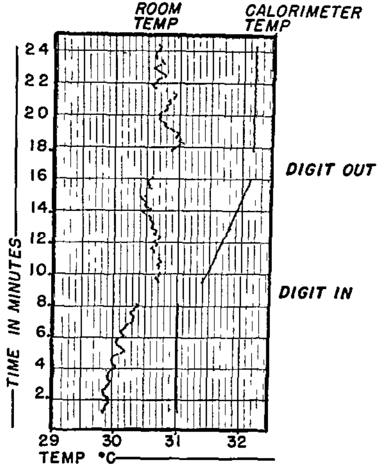


FIG 39C — A typical record of digital calorimetry (Mendlowitz[400b])

DIGITAL VASCULAR RESISTANCE AND INTRAVASCULAR BLOOD VISCOSITY

Peripheral resistance has in the past been measured by dividing pressure by flow and multiplying this value by a constant [38] This constant includes the so called viscosity factor and carries the implication that with unchanged resistance the relationship between pressure and flow with varying pressures is rectilinear It has however been demonstrated by many workers that especially in small blood vessels this relationship may not be represented by a straight line [3, 05, 06, 518] It has also been found that apparent viscosity[56] may not be a constant [48] but may change with changes in velocity [48, 63, 449] in caliber of the perfused vessels [48] and in the temperature[134, 388] and nature of the perfusate [48, 600] In 1951[399] Mendlowitz studied the pressure flow relationship in the digital circulation in an attempt to separate the various factors in the peripheral resistance in order to compare the abnormal with the normal circulation

If the vascular bed of a dog s leg is perfused with Ringer s solution or plasma the relationship between pressure and flow is rectilinear [600]

If venous pressure is subtracted from arterial pressure in the calculations a measure neglected by earlier workers[600] the straight line intercepts the pressure axis at or near zero. *Poiseuille's law*[466] *is then applicable*, the formula being

$$Q = \frac{P\pi r^4}{8l\eta} \qquad (1)$$

in which Q is the volume flow in cc./second, P the mean arterial pressure minus the venous pressure converted into dynes/sq. cm., r the radius of the tube in cm., l the length of the tube in cm., and η the viscosity in poises (dyne second sq. cm.). If r, l and η are fixed, the only variables are P and Q and the formula becomes the familiar Q = Pk in which k is a constant. This is clearly a rectilinear equation.

When blood is used as the perfusing fluid the relationship between *P and Q* has been interpreted by different workers to be rectilinear *with a* shifting intercept on the pressure axis[600], hyperbolic and *hence approaching* an asymptote[54, 55] or logarithmic[197, 95, 96, 451]. There are several possible factors involved in this deviation from the Poiseuilleian straight *line*. Increasing pressure may distend blood vessels progressively or open new *capillaries* especially at low velocity rates[94]. With maximum vasodilatation however the effect of pressure on the vessels becomes *minimal*. What is more curves similar to those seen *in vivo may be* obtained by perfusing glass tubes of appropriate diameter[464, 466]. *Changes in the* physical elasticity or compressibility of the cells and plasma are too small to account for the effects observed at low pressures[609]. The lower portion of the curve may however be affected by changes in alignment and distribution of cells and possibly by changes in their shapes at lower pressures. This is sometimes referred to as plasticity[339]. The slope of the upper portion of the curve is *modified* at vascular resistances prevailing in the peripheral circulation by the Fahraeus phenomenon[151]. *This* represents a *decrease in* apparent viscosity with decreasing tube caliber below a critical radius. This is caused by proportionate increase in the peripheral zone of plasma which is less viscous than blood, the cells being crowded into the center of the stream. It is this effect which creates considerable discrepancy between viscosity determined in vivo and that found in vitro. It may also be responsible for the lower hematocrit of digital blood as compared with *venous* blood[187]. It has also been shown however that increasing vasoconstriction in the hind limb of the dog increases apparent viscosity[453]. *Because* of the simultaneously increased intercept of the major pressure flow slope on the pressure axis, this increase in viscosity is greatest at very low rates of flow. At such low rates of flow moreover ischemia can cause capillary dilatation with variable changes in diffusion from capillaries to tissues which may modify pressure

flow curves by changing the red cell and plasma protein concentration of the blood [204] Such changes in diffusion are theoretically possible at higher flow rates[314] but are probably unimportant in the terminal digit where most of the flow is through arteriovenous anastomoses Another factor which may modify pressure flow curves is the critical closing pressure which increases with increasing vasomotor tone [90, 436]

Logarithmic formulas [04, 325, 453] for the pressure flow relationship have been fitted to empiric data and have been found to be $Q = aP^k$ or $Q = (P/m)^n$ [06] in which a and k or m and n are constants In such a formula the exponential function k or n is the plasticity factor and a or m the variables of Poiseuille s law,[466] r l, and η together with the Fahraeus phenomenon factor The exact relationship of these factors has not yet been worked out physically although Lamport[324] has recently presented a logarithmic formula incorporating the factor of caliber The constant k, *has been found to vary from 1 4 to 1 8 in animal perfusion experiments* [2, 3] It must be remembered, however that these formulas are derived from data obtained by the perfusion of vascular beds in which the preponderance of flow is through capillaries [204] In the human digital circulation in which sympathetic vasomotor tone is released the preponderance of flow is through arteriovenous anastomoses [1, 399] It therefore becomes necessary to determine the character of the pressure flow curve in the human digital circulation to see if any difference can be detected between such curves and those obtained in animals and also to see if these pressure flow relationships can be used to analyze digital vascular resistance

To this end studies were made after stabilization of the circulation by indirect heating on a normal subject on a patient with severe polycythemia vera and on several patients with hypertension [398, 399] Pressure flow relationships at various digital arterial pressures were *obtained by* graded occlusion of the brachial artery A blood pressure cuff could not be used because it introduced the factor of variable and progressive in*crease in venous pressure* A clamp was therefore devised that would produce a given degree of compression of the brachial artery without compressing the veins (fig 40) [399]

That no significant increase in venous pressure occurred after compressing the brachial artery with this clamp was confirmed repeatedly by direct and indirect venous pressure determination [399] Direct measurement of brachial systolic and diastolic and planimetric mean pressures with a strain gage manometer in several cases showed that the arithmetic mean corresponded fairly well with the true mean or was slightly higher [399] This relationship changed very little if at all with brachial artery compression [399] *What is more such compression produced no change in the eryth*rocyte concentration and hence viscosity of the perfusing arterial blood [399]

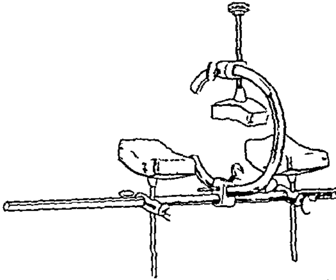


FIG 40—Arterial compression clamp (Mendlowitz[399] courtesy Grune & Stratton)

One possible source of error was the subtraction of 6 mm Hg from the mean arterial pressure as average venous pressure With decreasing digital arterial pressure the digital venous pressure might well fall[399] What is more the venous pressure in veins draining arteriovenous anastomoses might be somewhat higher than in those draining capillaries* Also the venous pressure might act over a wider cross sectional area than the arterial pressure which would create an error in estimating resistance in dynes (p 85)[399] These factors however appeared to be small enough to be negligible

The validity of the technic for measuring blood flow was exhaustively established elsewhere[397] Repeated pressure flow determinations at heart level[390, 394] after maximal vasodilatation by indirect heating were made on different days in the same subject[389, 397] It had been demonstrated that in any given individual this relationship was nearly identical from day to day Only those experiments were accepted in which the brachial pressure from day to day was stable and in which the digital pressures before and after the flow observations remained unchanged[399] That inhibition of sympathetic nerve discharge could be satisfactorily effected in the upper extremity by indirect heating was demonstrated by Arnott and Macfie (p 65)[22]

When our results were plotted by the method of the least squares[455] on logarithmic paper using the formula $Q = aP^k$ k was found to vary from 0 8 to 1 2[399] and not from 1 4 to 1 8 as had been found in animal

* Te mm Hg has been shown to be the average venous pressure in the dorsum of the hand normally (p)

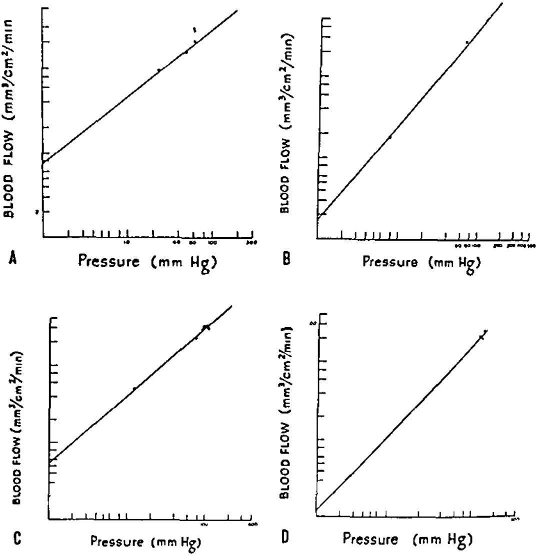


FIG 41 —Logarithmic pressure-flow relationship A normal (M M) $Q = 7.491\ P^{0.78842}$ B polycythemia (M K) $Q = 1.678\ P^{1.1293}$ C mild essential hypertension (M G) $Q = 5.358\ P^{0.8101}$ D severe essential hypertension (A B) $Q = 1.155\ P^{1.08172}$ (Mendlowitz [399] courtesy Grune & Stratton)

experiments [325] Typical graphs are presented in figure 41 It is clear that when K is 1 or nearly 1 we are dealing with a rectilinear rather than a curvilinear relationship [399] The reason for the discrepancy between these studies and animal perfusion experiments probably lies in the fact that in the fingertip flow through arteriovenous anastomoses predominates over that through capillaries [398, 399]

The results of observations in normal polycythemic and hypertensive subjects were hence plotted on cartesian coordinates (fig 42) [455] The rectilinear fit was as good as the logarithmic and the least squares method was employed to determine straight line regressions [455] The intercepts of these lines hovered around zero [399] The deviations of the points from the pres

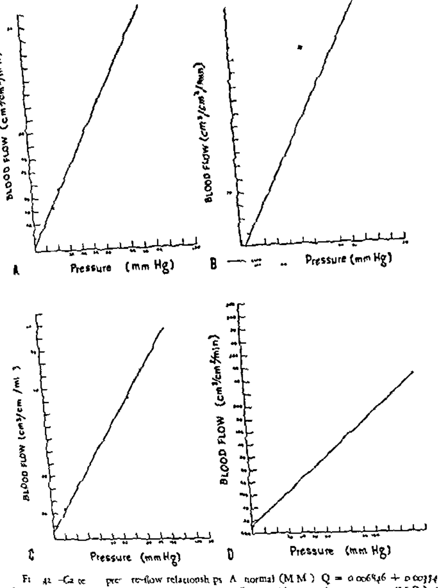


Fig. 42.—Calculated pressure-flow relationships A normal (M M) Q = 0.006846 + 0.003345 P B polycythemia (M K) Q = 0.013384 + 0.003705 P C mild essential hypertension (M G) Q = 0.00974 + [illegible]030 P D severe essential hypertension (A D) Q = 0.0011805 + 0.001 06 P (Mendlowitz,[309] courtesy Grune & Stratton)

sure flow lines were due to slight fluctuations in sympathetic nerve discharge to such errors as are inherent in the method as well as to the fact that arithmetic and true mean pressures do not always coincide [299] The return of the pressure flow ratio to normal in the polycythemic patient after repeated phlebotomy was nicely demonstrated [294] Consideration of probable error however indicated that the exact intercepts on the pres

sure axis could not be accurately determined from these lines, especially in hypertension and could be considered to be 0 ± 10 mm Hg [399]

If these observations are valid and the error involved in disregarding the intercepts on the pressure axis is sufficiently small, it becomes possible to apply Poiseuille s law[466] to the digital circulation [399] In formula 1 η represents the viscosity of the blood Whittaker and Winton[600] showed in animal perfusion experiments that normal intravascular blood viscosity is approximately 2 2 times that of Ringer s solution at a temperature of 37 C The changes in viscosity, moreover, with varying erythrocyte concentration demonstrated by these workers in animals were reproduced in the human digital circulation[394] [395] (fig 43) Since the viscosity of water [48] or Ringer s solution at 37 C is 0 0069 that of blood is 0 015 poises There is an *insignificant error involved here because the average* temperature of the blood in the fingertip is 33 to 34 rather than 37 C [134] The increase in apparent viscosity with vasoconstriction described by Pappenheimer and Maes[453] in animal perfusion experiments was due *chiefly to the increasing intercept of the pressure flow slope on the pressure* axis Since such a shift is minimal in the digital circulation, if it occurs

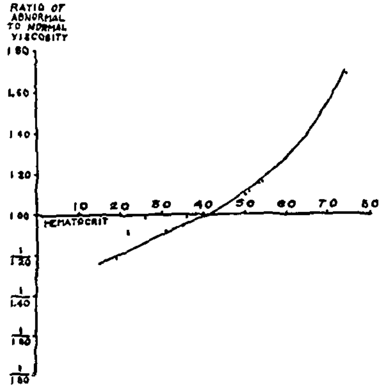


FIG 43 —The black dots rep sent observed changes in human intra ascular viscosity with arying erythrocyte concentrations in six patients The curve is drawn in from Whittaker and Winton[60] making allowances for a slightly high r normal *hematocrit of dogs and for the fact that flow is expressed* olu metrically rather than gravimetrically (Mendlo itz [395] courtesy of J Clin Investigation)

at all the apparent viscosity can fairly safely be assumed to be 2 2 times that of water or Ringer s solution [399] It still remains necessary to demonstrate this relationship by perfusion experiments on amputated human extremities [399]

The only remaining unknowns in the equation are length and caliber These two factors together represent the physical configuration of the digital blood vessels Thus transposing in equation 1

$$\frac{\pi r^4}{8l} = \frac{Q\eta}{P} \tag{2}$$

The vascular configuration volume index is represented by $\frac{\pi r^4}{8l}$ Thus, in a typical calculation, if the arithmetic mean digital arterial pressure minus venous pressure is 52 mm Hg and the flow 0 0047 cc / second/sq cm of skin 5 2 cm multiplied by 13 6 (specific gravity of mercury) and by 980 cm second² (acceleration due to gravity) equals 69 306 dynes/sq cm For normal blood η is 0 015 dyne second/sq cm Hence the vascular configuration volume index is

$$\frac{\frac{0\ 0047\ cc}{sec} \cdot \frac{0\ 015\ dyne\ sec}{sq\ cm}}{\frac{69\ 306\ dynes}{sq\ cm}} = 0\ 0000000001010\ cc$$

or 1010 cu μ [399] Calculations of this index[399] based on thirty four normal subjects twenty five cases of essential hypertension, and six cases of malignant hypertension are presented in table 14 Calculations in a typical case of polycythemia [399] before and after repeated phlebotomy are also presented in table 14 These results are representative of those calculated in seven other cases of polycythemia [391, 395, 399]

Separation of the factor of length from that of caliber is impossible in an irregularly branching system [328] Such separation can however be effected theoretically as follows[399] If it is assumed that Poiseuille s law [188] applies to the systemic circulation as a whole * the force at the sinuses of Valsalva would be represented by pressure in dynes/sq cm multiplied by the aortic cross sectional area in square centimeters If the cross sectional area as estimated roentgenographically is approximately 13 sq cm at a flow of 80 cc /second and a mean pressure of 100 mm Hg a theoretic length factor[33] can be calculated from equation 2 to be about 7 kil This means that if the aorta were a uniform bore horizontal tube 7 kil long it would offer the same resistance as is offered by the entire systemic arterial tree provided the viscosity of the blood were

* Th p [illegible] city f ctor mod fies Po seu lle s law in the sy tem c culat on and the fig es are in [illegible] u ate to that ext [illegible]

Table 14 — Dimensions and Resistance of the Digital Vascular Bed (Mendlowitz [399])

Determination	Normal range	Essential hypertensive range	Malignant hypertensive range	Polycythemia (M K)	
				Hematocrit [illegible]%	Postphlebotomy hematocrit 44%
Digital vascular volume index/cm² of skin in cu μ	1010–653	653–308	308–177	11,7	946
Estimated length factor for one digital artery in cm assuming average radius of 0 03 cm and adjusting value to average size fingertip	55 6	55 6	55 6	56 6	55 6
Initial caliber of a single digital artery (in cm of radius) adjusted to average size fingertip	0 031–0 028	0 028–0 023	0 023 0 020	0 033	0 031
Resistance in dyne sec /cm⁵ of a vascular bed perfused by a single digital artery (adjusting value to average size fingertip)	2 287 000–3 420 800	3 420 800–7 219 300	7 [illegible]19 300–12 568 [illegible]00	3 275 200	2 343 600
Resistance in dyne sec /cc of flow of a vascular bed perfused by a *single digital artery (adjusting* value to average size fingertip)	6 757–8 421	8 421–11 992	11 992–15 786	11 199	6 925
Resistance in dynes/cm² of cross sectional area in a vascular bed perfused by a single digital artery (adjusting value to average size fingertip)	69 306–111 955	111 955 211 915	203 918–226 576	95 962	[illegible]6 636
Resistance in dynes in a vascular bed perfused by a single digital artery (adjusting value to average size fingertip)	[illegible]35–301	301–406	386–357	320	230

kept unchanged It is also very probable that this length factor does not change much for any given vascular bed Hence if a length factor is established for a vascular bed in this way the initial cross sectional area can be calculated back *from the formula and its normal range of variation* estimated [399]

The same process may be applied to the two digital arteries where Poiseuille s law[466] does apply [399] Roentgenograms of these arteries in preliminary observations reveal an approximate initial diameter after vasodilatation of 0 06 cm each as they enter the terminal segment of the finger [17] [399] and the length factor in each entire digital circulation can be calculated to be approximately 55 6 cm This means that if each digital artery were a uniform horizontal tube 55 6 cm *long it would offer* a resistance comparable to that offered by the entire digital vascular bed supplied by that artery provided the apparent viscosity remained unchanged [399] Both digital arteries are assumed to be equal in caliber and

since caliber varies with the surface area perfused a size factor, average surface/actual surface has been incorporated in the calculation [399] The variations in caliber[399] presented in table 14 may be modified when more extensive radiographic data on digital arteries in the dilated state become available

To calculate resistance formula 1 may be rearranged as follows

$$\frac{P}{Q} = \frac{8l\eta}{\pi r^4} \tag{3}$$

Since P is expressed in dynes/sq cm and Q in cc /second P/Q is expressed in dyne second/cm 5 This method was introduced by Boger and Wezler[41] and is commonly used to measure peripheral resistance When such resistance is calculated for the human systemic circulation as a whole[416] it is 539 to 1130 dyne second cm 5 For the rabbit[410] it varies from 11 670 to 12 590 and for the vascular bed of a single digital artery [399] in the normal fingertip from 2 287 000 to 3 420 800 dyne second/cm 5 The normal and abnormal variations in digital vascular resistance calculated in this way[399] are presented in table 14 Superficially it seems incredible that the resistance of systemic vessels in a rabbit or in a fingertip should be so much greater than the resistance of the entire human systemic circulation unless one remembers that the expression dyne second/cm 5 measures resistance in dynes per unit of blood flow and per unit of cross sectional area [399] *It is* therefore relative to the actual blood flow and actual cross sectional area [399]

The resistance in dynes can be measured only by multiplying the resistance in dyne second cm 5 by the actual blood flow and cross sectional area [399] Thus if equation 3 is converted into physical units

$$\frac{\text{dynes sq cm}}{\text{cc second}} = \frac{\text{cm dyne second sq cm}}{\text{cm}^4}$$

or

$$\frac{\text{dyne second}}{\text{cm}^5} = \frac{\text{dyne second}}{\text{cm}^5} \tag{4}$$

Multiplying both sides of the equation by the actual Q in cc /second and the actual cross sectional area in sq cm we have

$$\frac{\text{dyne second}}{\text{cm}^5} \quad \frac{\text{cc}}{\text{second}} \quad \text{sq cm} = \frac{\text{dyne second}}{\text{cm}^5} \quad \frac{\text{cc}}{\text{second}} \quad \text{sq cm}$$

or

$$\text{dynes} = \text{dyne}$$

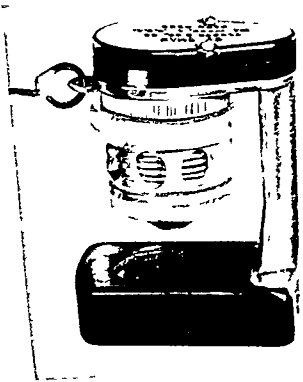
Thus the force in dynes exerted by the pressure acting over the initial cross sectional area is equal to the resistance in dynes provided the flow is constant [3] In a system in dynamic equilibrium force and opposing re

TABLE 14 — *Dimensions and Resistance of the Digital Vascular Bed (Mendlowitz [399])*

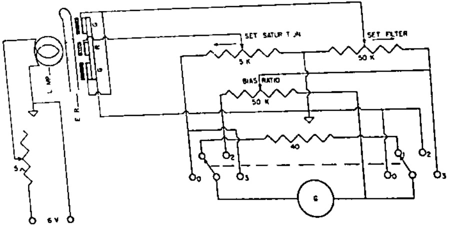
Determination	Normal range	Essential hypertensive range	Malignant hypertensive range	Polycythemia (M K)	
				Hematocrit 2[illegible]	Post phlebotomy hematocrit 44[illegible]
Digital vascular volume index/cm² of skin in cu μ	1010–653	653–308	308–177	1177	946
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Resistance in dyne sec /cm⁶ of a vascular bed perfused by a single digital artery (adjusting value to average size fingertip)	2 287 000–3 420 800	3 420 800–7 219 300	7 219 300–12 568 700	3 275 200	2 343 600
Resistance in dyne sec /cc of flow of a vascular bed perfused by a single digital artery (adjusting value to average size fingertip)	6 757–8 421	8 421–11 992	11 992–15 86	11 199	6 925
Resistance in dynes/cm² of cross sectional area in a vascular bed perfused by a single digital artery (adjusting value to average size finger tip)	69 306–111 955	111 955–211 915	203 918–226 576	95 962	,6 636
Resistance in dynes in a vascular bed *perfused by a single digital artery* (adjusting value to average size fingertip)	235 301	301–406	386–357	320	230

kept unchanged It is also very probable that this length factor does not change much for any given vascular bed Hence if a length factor is established for a vascular bed in this way the initial cross sectional area *can be calculated back from the formula and its normal range of variation* estimated [399]

The same process may be applied to the two digital arteries where Poiseuille s law [466] does apply [399] Roentgenograms of these arteries in preliminary observations reveal an approximate initial diameter after vasodilatation of 0 06 cm each as they enter the terminal segment of the finger,[17, 399] and the length factor in each entire digital circulation can be calculated to be approximately 55 6 *cm This means that if each digital* artery were a uniform horizontal tube 55 6 cm long it would offer a *resistance* comparable to that offered by the entire digital vascular bed supplied by that artery provided the apparent viscosity remained un changed [399] Both digital arteries are assumed to be equal in caliber and



F G 44A —Earpie e for M llik n oximeter (Comr and Wood ² co rte y The Yearbook Pub lishers Inc)



F G 44B —Ci c it d ag m of M ll kan compensated ci cuit oximeter G galvanometer (sensitivity such that 0 0006 μ mp c e defl ct on f 1 mm) R red photoelect ic cell co ered by Wratten 29 F filte G g n ph toelect c cell co ered by Wratten 61 N filter k = 1000 ohms (Comroe and W xd c x t y th Ye book Publishers I c)

sistance in dynes must be exactly equal.[399] Such resistance is the resultant of the frictional forces in the blood stream acting in a direction opposite to that of pressure.[399] *To calculate force and hence resistance in dynes, it can* be seen from equation 4 that the pressure in dynes/sq. cm. may be multiplied by the calculated initial digital arterial cross sectional area in square centimeters, the flow factor being cancelled.[399]

It is to be noted that resistance in dynes varies directly with pressure and directly with cross sectional area.[399] Since the cross sectional area determines flow if the other factors remain constant, resistance in dynes varies directly rather than inversely with flow. The digital vascular resistance in dynes (table 14) now becomes an intelligible proportion of the total systemic resistance, which can be calculated from the total *systemic force at the sinuses of Valsalva* to be approximately 1 732 640 dynes.[399]* Such resistance is proportionately much higher per gram of fingertip than per gram of average tissue because of the greatly increased flow in the fingertip made possible by the arteriovenous anastomoses.[399]

Resistance and force in dynes can also each be divided by the actual cross sectional area to give

$$\frac{\text{dynes}}{\text{sq. cm.}} = \frac{\text{dynes}}{\text{sq. cm.}}$$

It will be recognized that in this sense pressure per unit of cross sectional area is exactly equal to resistance per unit of cross sectional area.[399] If the resistance in dynes seconds/cm^5 is divided by the actual cross sectional area in cm., on the other hand, we have

$$\frac{\text{dynes second}}{\text{cc}} = \frac{\text{dynes second}}{\text{cc}}$$

or

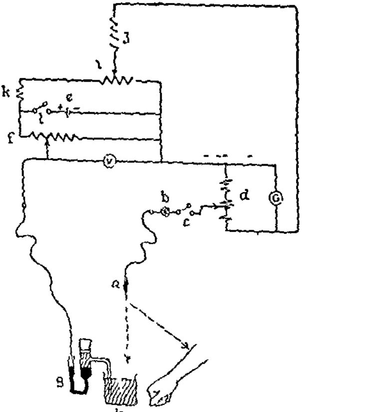
$$\text{dynes/unit of flow} = \text{dynes/unit of flow}$$

This simply serves to express the resistance in terms of average or unit flow and is just as informative but more intelligible than the expression dyne second/cm^5.[401]

It can be seen as determined from table 14 that vascular volume index and caliber after inhibition of sympathetic nerve discharge are decreased and resistance is increased in established hypertension.[399] Also, a critical point in vascular volume index, caliber, and resistance in dyne second/cm^5 or in dynes/unit of flow can be found beyond which the cases of malignant hypertension fall.[399] Resistance in dynes is more variable in malignant hypertension because of the variable decrease in flow and caliber.[399] Resistance per unit of cross sectional area is also more variable in malig-

* See footnote on page 83

Recently indirect methods for measuring blood and tissue oxygen tension have been introduced each with some applicability to the digital circulation The *oximeter* measures average oxygen tension in the blood [110] It is a photoelectric device with filters designed to record the concentration of oxyhemoglobin in the blood as it courses through the part (fig 44) Since both arteries and veins are included in the tissues transilluminated it is clear that only average blood oxygen can be measured [111] This average is probably not a true arteriovenous mean but lies somewhere between the two extremes depending on circulatory conditions Under conditions of inhibition of sympathetic nerve discharge this average is closer in the finger and also in the ear lobe to the oxygen content of the arterial blood [11] If these conditions are maintained it is possible in this



F 46 —W ng diagr m of cir uit of pol *ograph* (M ntgomery and Horwitz [33] cou t sy J Cl n In e t g)

Leg nd a = electrode t p (cathode) b = electro witch (controlling six electrodes) ... = electrode ... d = Ay ton shunt (R b n no 243) (r istance 0 to 65 000 ohm) e = dry ell (1 5 olt) f = ... ble resi tance (1 000 ohms) g = c lomel half-cell (anode) contain ng 0 90 NaCl h = 0 9 per ent N Cl in be ker i = variable re tance (1 000 000 oh ns) k = fi ed re istance (40 000 ohm) l = ma w tch G = g l *rometer* (Rubic m no 3419) V = oltmeter

nant hypertension[399] In polycythemia, on the other hand if the viscosit factor is corrected in accordance with erythrocyte concentration th vascular volume index and caliber are approximately normal or slightl above normal despite moderately increased resistance[395, 399] After phle botomy all these values become normal[395, 399]

OXYGEN EXCHANGE

The exchange of oxygen in the digit is difficult to study and the result are of questionable reliability The reason for this lies partly in the tech nical difficulty in obtaining reliable samples of digital venous blood In addition, the rapid fluctuations in flow make it essential that flow and *arteriovenous oxygen determination be simultaneous if any conclusion is* to be drawn as to the oxygen consumption of the tissues of the digit[401] Also after complete dilatation of the arteriovenous anastomoses the arteriovenous oxygen difference becomes so small that it falls within the experimental error of the method[553] making the error of the difference very large[401]

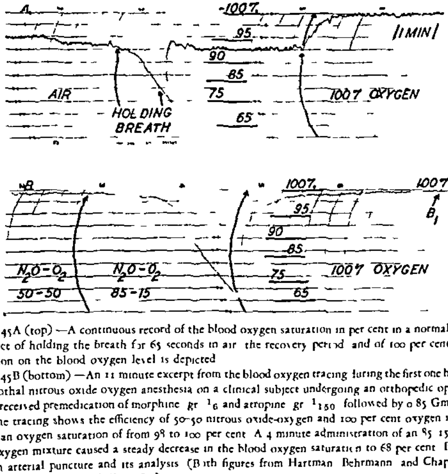


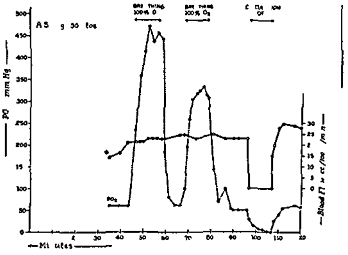
Fig 45A (top) —A continuous record of the blood oxygen saturation in per cent in a normal subject The effect of holding the breath for 65 seconds in air the recovery period and of 100 per cent oxygen inhalation on the blood oxygen level is depicted

Fig 45B (bottom) —An 11 minute excerpt from the blood oxygen tracing during the first one half hour of Pentothal nitrous oxide oxygen anesthesia on a clinical subject undergoing an orthopedic operation Patient received premedication of morphine gr 1/6 and atropine gr 1/150 followed by 0 85 Gm pentothal The tracing shows the efficiency of 50-50 nitrous oxide-oxygen and 100 per cent oxygen in maintaining an oxygen saturation of from 98 to 100 per cent A 4 minute administration of an 85 15 nitrous oxide-oxygen mixture caused a steady decrease in the blood oxygen saturation to 68 per cent B represents an arterial puncture and its analysis (Both figures from Hartman Behrmann and Chapman [illegible] courtesy The Williams & Wilkins Co)

Montgomery and Horwitz[473] have recently developed a polarographic needle electrode capable of measuring subcutaneous oxygen tension (fig 46) A traumatic procedure in the highly sensitive and richly vascular digital circulation is undesirable and subject to difficulties in interpretation [471] Nevertheless changes in the tissue oxygen tension with changes in vascular caliber as well as in arterial blood oxygen content can be nicely recorded (fig 47)



way to obtain a continuous record of arterial blood oxygen content (fig 45) [46] The ear lobe is usually preferred to the finger however, for this purpose The metabolism of the skin can be estimated from the rate of change in color produced by the reduction of oxyhemoglobin during a period of arterial occlusion [87]



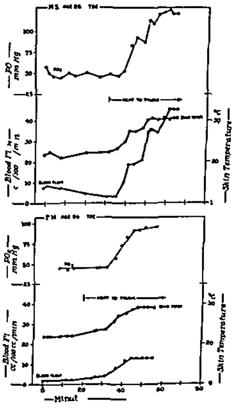


Fig 47A (top) —Effects of oxygen inhalation and of arrest of circulation on oxygen tension of skin of toe

Fig 47B (bottom) —Effect of physiologic variations in blood flow upon oxygen tension of skin of toe (Both figures from Montgomery and Horwitz [22] courtesy J Clin Investigation)

T[illegible] 25 —St[illegible] A[illegible]alysis [illegible] D[illegible] Ob[illegible] [illegible] with Thromboangiitis Obliterans Compared with th[illegible] from Normal Subjects (Mendlowitz and Abr[illegible])

	No. of cases	Cutaneous blood flow (cc/m[illegible]/min)					
		Range	Mean	Standard deviation	Standard error of m[illegible]	[illegible]	[illegible] ratio
Normal	24	0 15-0 20	0 2	0 041	0 009		
Thromboangiitis obliterans	35	0 01-0 23	0 10	0 047	0 012	0 012	9 2

T[illegible] —St[illegible] Thromboangiitis Obliterans [illegible] Upper Extremities Showing that Decreased Flow is Caused by Decreased Pressure [illegible] Remaining Limb [illegible] (M[illegible])

[illegible]	Age and sex	Diagnosis	Duration	Brachial B P (mm Hg)	Dig B P (mm Hg)	Dig B F (cc/m[illegible])	Dig [illegible]res[illegible]
I S	33 M	Thromboangiitis obliterans	3 years	120/8	35/25[?]	0 13	54
W D	32 M	Thromboangiitis obliterans	3 years	128/98	65/54	0 15	105

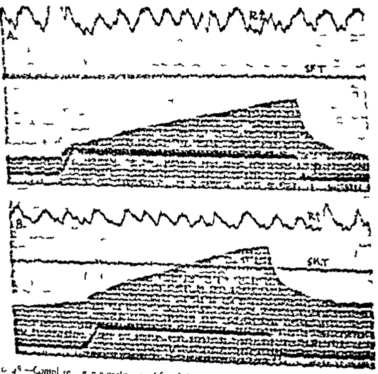


Fig 48—Complete [illegible] occlusion of first left [illegible] A Venous congestion during rest Skin temperature [illegible] 8 C B Fully dilated Skin temperature at 29 3 C Reduction of original tracing [illegible] Goet[illegible] courtesy Am He[illegible])

6

PERIPHERAL VASCULAR DISEASES

PERIPHERAL vascular disease may affect the circulation at different sites and in various combinations of pathologic changes [1, 309] The veins may be obstructed as by thrombophlebitis or by the increased back pressure incidental to such conditions as varicose veins [17] The capillaries may be obstructed by clot compressed by edema, or constricted by inflammatory or scar tissue and this also applied to the arteriovenous anastomoses [1] The arteries may be affected in their terminal portions as in frostbite [40] The digital arteries themselves may be obstructed as in Raynaud s disease[348] or mean pressure in the digital arteries may be reduced because of obstruction stenosis, or coarctation in the larger arterial channels One of the most important forms of arterial occlusion is by thrombosis [17] Embolization is much less common Arteries may also be narrowed by the process of arteriosclerosis and arteriolosclerosis and they may be constricted by scar tissue as in scleroderma [17]

THROMBOANGIITIS OBLITERANS

In thromboangiitis obliterans initial arterial obstruction usually occurs in the medium sized arteries of the upper or lower extremities [76, 693] At this stage pressure is low in the digital arteries [393, 404] The gradient of pressure is steep in the upper or lower extremities as a whole and flow is usually reduced[68, 315] in proportion to the decrease in pressure the digital vascular resistance remaining unchanged [393] When secondary changes take place in the tissues of the digits because of ischemia secondary scleroderma with additional compression of digital vessels of all kinds by scar tissue may occur [17, 80, 81] Tables 15 and 16 summarize data obtained in the circulation of fingers and toes in patients with thrombo

TABLE 17 —The Dig t l Circulatio in Scleroderma (Mendlowitz[101])

Pat t	Ag d sex	After d ect heat g nd TEAC (5 mg/kg)			
		Br hial B P (mm Hg)	D g tal B P (mm Hg)	D gital Blood Flow (als m ( ) (c m m n)	
				F ng r	Gre t toe
1	39 F	102/72	96/68	0 23	
	49 F	198/118	182/90	0 14	
3	37 F	126/88	108/62	0 19	
4	51 F	123/65	110/45	0 14	
5	43 F	94/58	68/55	0 09	
6	56 M	120/90	90/6	0 02	
7	48 F	112/74	58/48	0 03	
8	65 M	174/78		0 05	
9	23 F	80/62		0 07	0 04
10	6 F	96/38		0 336 L	0 203 L
1	42 F	98/48	52/?	0 044	
12	21 F	18/76	78/36	0 413	
13	52 F	94/50	42/20	0 056	
4	46 M	110/80		0 133 R	0 09 L
5	38 M	10/74			0 14 R

lation tissue scar contracture ischemia necrosis and granulation tis sue [101] Subcutaneous calcinosis and pigmentation of the skin are late sequelae [17 100]

Sympathectomy is efficacious in this disease[70] only by its effect on associated neurogenic vasomotor tone [1] Digital blood flow after release of such tone by heat and tettaethylammonium chloride is found decreased and digital vascular resistance is increased from the normal sometimes to a tremendous extent[393 401 404] (table 17) Hypertension is not an associ ated feature because usually only the subcutis is involved [401] visceral lesions being a late effect and not universal in the average case Raynaud s attacks may be a feature of scleroderma (p 96) [280 281 284]

A word should be said about scleredema adultorum [372 451] This disease also involves the subcutaneous tissues and at times the viscera but usually spares the hands and feet Digital circulation studies done in a few such cases were normal

RAYNAUD S DISEASE

Raynaud s disease[479 483] is manifested by spasmodic complete usually symmetrical ischemia of the fingertips and/or toes [18 356] The Raynaud s spasm can be produced only by complete or nearly complete occlusion of the digital arteries [401] It probably occurs whenever the intra arterial pressure falls below the critical closing pressure [404 436] In the ordinary normal digital artery extreme sympathetic nervous stimulation as pro duced by certain emotional reactions or by cold will cause a marked

angiitis obliterans, after inhibition of sympathetic nerve discharge[391, 404] In the presence of this disease reactive hyperemia to a period of vascular obstruction also produces lower flow when compared with the normal[6, 5]

It has also been shown that blood flow as measured plethysmographically, as well as volume pulse contour is altered in occlusive arterial disease[579] (fig 48) In addition especially in the advanced stage capillary changes take place and the oxygen tension of the skin[4, 3] and venous blood[584] is decreased Patients with thromboangiitis obliterans may show a variable degree of vasospasm as measured by the various methods for detecting changes in blood flow and blood pressure before and after inhibition of sympathetic nerve discharge[4, 6, 604] It is difficult to ascertain whether such vasospasm is generally greater than or equal to that encountered *in the population as a whole*

Thromboangiitis obliterans may involve smaller as well as larger arteries although this rarely occurs as an early phenomenon[17] If the digital vessels are involved, Raynaud s phenomenon may be observed[17] (p 96) Venous thrombosis in the form of thrombophlebitis migrans is often encountered[7] but these manifestations of the disease rarely have any significant effect on the digital circulation except for transient inhibition of sympathetic nerve discharge produced reflexly[35] or by associated fever[609]

SCLERODERMA AND SCLEREDEMA

Scleroderma is a generalized disease chiefly affecting skin and subcutaneous tissues as a whole[444, 447] It is chronically progressive and is now generally classified with the so called collagen diseases[306, 307] Any diffuse process which causes generalized injury to subcutaneous tissue can produce scleroderma[474] It is for example occasionally seen as a sequel of acute glomerulonephritis[401] acute disseminated lupus erythematosus[30, 306, 407] and acute rheumatic fever[401] or rheumatoid arthritis[401] In most cases however the cause of the injury to subcutaneous tissue remains unknown Cold may in some way be implicated but it is not clearly understood by what mechanism[401] Endocrine factors are probably also important in the pathogenesis of scleroderma[17] Esophageal and pulmonary lesions are among the more common visceral features[444, 447] of the disease and joint symptoms may be secondary to contractures

Once a sufficient amount of granulation and then scar tissue is produced in the subcutis the disease is self perpetuating and slowly progressive[474] The reason for this is the tendency for scar tissue to contract and tighten the skin[470, 535] These contractures narrow blood vessels and in addition cause secondary thrombosis with resultant ischemia and further ischemic necrosis of subcutaneous tissue thus perpetuating the cycle of granu

TABLE 17—*The Digital Circulation in Scleroderma (Mendlowitz* [401])

Patient	Age and sex	After indirect heating and TEAC (5 mg/Kg)			
		Brachial B P (mm Hg)	Digital B P (mm Hg)	Digital Blood Flow	
				Finger	Great toe
1	39 F	102/[illegible]2	96/68	0 23	
2	49 F	198/118	[illegible]8/90	0 14	
3	37 F	126/88	108/62	0 19	
4	35 F	125/65	110/45	0 14	
5	43 F	94/58	68/55	0 09	
6	56 M	120/90	90/65	0 02	
7	48 F	112/74	59/49	0 03	
8	65 M	[illegible]/8		0 05	
9	23 F	80/62		0 07	0 04
[illegible]0	6 F	96/38		0 336 L	0 205 L
11	42 F	88/48	32/[illegible]	0 044	
[illegible]2	21 F	118/76	73/36	0 453	
[illegible]3	52 F	94/50	42/20	0 056	
[illegible]4	46 M	1[illegible]0/80		0 133 R	0 09 L
[illegible]5	38 M	150/74			0 14 R

lation tissue scar contracture ischemia necrosis and granulation tissue [401] Subcutaneous calcinosis and pigmentation of the skin are late sequelae [17, 109]

Sympathectomy is efficacious in this disease[70] only by its effect on associated neurogenic vasomotor tone [1] Digital blood flow after release of such tone by heat and tetraethylammonium chloride is found decreased and digital vascular resistance is increased from the normal sometimes to a tremendous extent[393, 401, 404] (table 17) Hypertension is not an associated feature because usually only the subcutis is involved [401] visceral lesions being a late effect and not universal in the average case Raynaud s attacks may be a feature of scleroderma (p 96) [280, 281, 354]

A word should be said about scleredema adultorum [372, 431] This disease also involves the subcutaneous tissues and at times the viscera but usually spares the hands and feet Digital circulation studies done in a few such cases were normal

RAYNAUD S DISEASE

Raynaud s disease[479, 480] is manifested by spasmodic complete usually symmetrical ischemia of the fingertips and/or toes [18, 366] The Raynaud s spasm can be produced only by complete or nearly complete occlusion of the digital arteries [4 1] It probably occurs whenever the intra arterial pressure falls below the critical closing pressure [90, 436] In the ordinary normal digital artery extreme sympathetic nervous stimulation as produced by certain emotional reactions or by cold will cause a marked

decrease in blood flow in the digits but rarely to the level of complete ischemia,[401] sometimes called digital syncope unless digital arterial pressure is very low A trickle of blood usually courses through the main digital arteries and probably also via bone collaterals to continue to supply the needs of the tissues [397, 401] These needs are curtailed by the decreased temperature of the digits [401] Capillary flow is also probably promoted by the complete or nearly complete closure of the arteriovenous anastomoses which are extraordinarily responsive to sympathetic stimulation [401]

If the digital arteries are damaged, [53] however, this damage consisting either of intravascular thrombosis in various stages of organization or of arteriosclerosis [348] sympathetic nerve stimulation can cause a sufficient reduction in digital pressure and flow by spasm superimposed on thrombosis or sclerotic narrowing to produce complete ischemia or the digital syncope characteristic of a Raynaud s attack [361] During such syncope flow ceases[489] and capillary pressure drops to from 5 to 10 mm Hg [14, 37]

The causes of Raynaud s disease are many [79] In the susceptible individual cold itself may penetrate and damage vessels sufficiently to produce the characteristic syndrome [17, 401] Mechanical injuries to digital vessels may be produced in hydraulic drillers [38] or by lacerations[401] and also result in Raynaud s disease In addition any more generalized thrombotic disease such as thromboangiitis obliterans or arteriosclerosis obliterans may cause Raynaud s attacks if the digital arteries become involved [17, 401] It is also possible that small emboli may involve the digital arteries [401] these emboli having their origin in the heart or in thromboses of larger *arteries as in aortic or subclavian aneurysm* [331] scalenus anticus syndrome,[43, 44] the hyperabduction syndrome [50] Sudeck s atrophy [30, 56, 564] etc It is often difficult pathologically to distinguish between local *thrombosis and embolism Scleroderma which primarily involves the* subcutaneous tissues and causes scarring may constrict the digital arteries and eventually cause sufficient constriction by this process and by secondary thrombosis *to cause Raynaud s attacks to appear* [17, 354] *Any unusual* tendency of the blood to coagulate on exposure to cold favors the appearance of Raynaud s disease produced by thrombosis in the digital arteries Raynaud s *phenomenon is therefore seen in patients with cryo*globulinemia[36] and with increased cold agglutination [545] These conditions may be idiopathic or may be associated with multiple myeloma[36] or subacute bacterial *endocarditis*[36] *and with hemolytic anemia or virus* pneumonia respectively [548] Generalized thrombophilia as in lupus erythematosus [307, 538] periarteritis nodosa [401] megakaryocytic leukemia [471] polycythemia [401] *thrombocythemia* [401] *and the nephrotic syndrome* [401] may occasionally produce Raynaud s phenomenon

The immediate cause of the digital arterial syncope the Raynaud s attack itself[4 9, 480] is sympathetic nervous vasospasm usually superimposed on underlying obstructive arterial disease[351, 401] It is entirely possible that this sympathetic nervous vasospasm can cause vascular damage in itself[524, 5, 555] and favor the appearance of thrombosis in the digital arteries the usual initiating factor being cold[456] It is also possible that if the digital arterial pressure is sufficiently low because of either local or systemic conditions vasospasm may be sufficiently powerful to overcome intra arterial pressure and thus produce closure[90, 436] or a Raynaud s spasm Many people have neurogenic digital vasospasm[353] (acrocyanosis) for years however and with an occasional exception never develop Raynaud s disease One can therefore say that although vasospasm is a feature of Raynaud s disease such spasm does not necessarily cause the vascular injury usually responsible for the appearance of digital arterial syncope[401] Once vascular damage is produced however this in itself may stimulate vasospasm[348, 401] In addition it is very likely that every syncopal attack can cause further injury to the digital vessels in the form of thrombosis[346, 401] It is fo this reason that the disease is often progressive and self perpetuating[348, 401]

There are two important causes of sympathetic nervous digital vaso spasm cold and emotion[17] Cold causes greater acral vasospasm in some people than it does in others for various reasons Women are better in sulated by fat than men[43] but are often more susceptible[19] because of the inadequacy of clothing dictated by current fashion and because the epidermis is often thinner and therefore more permeable to the effect of cold[4 1] Also women s hands in the course of doing housework are often in greater contact with cold water than are men s[401] Illness starvation and low basal metabolism may be contributory factors in this increased susceptibility[401] In addition women are more volatile emotionally than men and this factor is of great importance in producing vasospasm[401] The maladjusted person often responds to what he or she feels is social inadequacy by cold clammy hands representing acral vasospasm[401] Sexual immaturity is an important factor and the Raynaud s patient is often one with sexual frustrations again more common in women than in men[401] If the vasospasm is more generalized there may be associated hypertension and the two conditions are not uncommonly seen together[401] Hyperten sion however tends to increas blood flow in the constricted circulation so that conditions favoring the development of Raynaud s disease are more likely to be found when the vasospasm is confined to the acral circulation and is associated with low blood pressure[401] It is important not to forget that circulating substances especially norepinephrine can also produce vasospasm and hence help precipitate a Raynaud s attack[153, 534] Pressure

and trauma along the course of arteries or sympathetic nerves, such as that produced by a prolapsed disc[17] tumor[0] fracture treated by plaster cast and followed by Sudeck's atrophy,[30, 56, 564] scalenus anticus syndrome[43, 44] cervical rib[9, 10, 430] or the hyperabduction syndrome,[50] may all produce vasospasm on the affected side[591] Raynaud's disease, however, is a much less common sequela and probably depends on coincident or prior damage to the digital arteries themselves,[401] or to reduction of digital arterial pressure below the critical closing level[90, 436]

Raynaud's disease should not be diagnosed in the absence of a clearcut history of blanching followed by cyanotic erythema[17, 401] Pain is a common associated feature This blanching can often be reproduced by submerging the hands or feet in water at a temperature of 12 to 15 C for 10 to 15 minutes but failure to reproduce these manifestations by this test[346] does not exclude the diagnosis (fig 49) Failure to produce blanching by subjecting the patient to a cold shower for a similar period of time is usually fairly good evidence of the absence of Raynaud's disease[17, 401] Raynaud's disease must be carefully distinguished from cold allergy[75] although the two conditions may occasionally coexist[401] In cold allergy, local immersion in cold water produces a somewhat erythematous pruritic edema but not true blanching whereas general immersion can produce syncope, and in a bather result in drowning[6]

If studies could be accomplished before and after the development of Raynaud's disease in every case, it is very likely that they would usually reveal some increase in intrinsic resistance in the digital circulation after inhibition of sympathetic nerve discharge as a reflection of the vascular damage[401] In early cases, however, this damage is not great enough to increase the resistance above the upper limit of the normal range As the disease advances however, blood flow is usually found to be unequivocally depressed and resistance proportionately elevated often to an extreme degree in very advanced cases (table 18)[393, 401, 404] There are also decreased pulsations as measured by the plethysmograph[579]

Vascular obstruction results in ischemic necrosis of tissues usually with sclerosis of fingertip skin and scarring of subcutaneous tissue[17, 80] Such scarring may be easily revealed by digital transillumination[567] This scarring is indistinguishable from that which occurs in scleroderma and in turn causes further constriction of digital vessels Secondary scleroderma produced in this way is nearly always confined to the fingers and toes in contrast to the more generalized process seen in diffuse scleroderma[80, 8] If vascular obstruction is sufficiently severe and prolonged gangrene of the fingers may ensue necessitating amputation[17, 479, 480]

Sympathectomy can be expected to eliminate only the vasospastic feature but this is of value in halting at least temporarily the progress

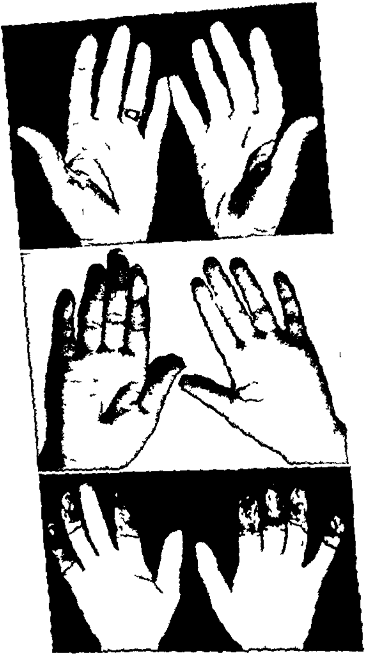


Fig 49 – A (top) Blanching of the *fingers in* Raynaud's disease B (middle) Cyanosis following blanching (left) compared with normal hand (right) (Allen Barker and Hines courtesy W B Saunders Co)

Fig 50 (bottom)—Frostbite (Davis Scarff Rogers and Dickinson courtesy Surg Gynec & Obst)

TABLE 18.—*The Digital Circulation in Raynaud's Disease* (Mendlowitz[401])

Patient	Age and sex	After indirect heating and TEAC (5 mg./Kg.)			
		Brachial B P (mm Hg)	Digital B P (mm Hg)	Digital blood flow (calorimetry) (cc /cm ² min)	
				Finger	Great toe
1	52 F	128/75	110/66	0 22	
2	23 F	112/78	110/65	0 20	
3	46 F	122/82	110/68	0 19	
4	45 M	116/84	74/54?	0 01	
5	36 M	122/72		0 24 3 L	0 14 R
				0 23 3 R	0 10 L
6	36 M	122/84		0 29	0 13
7	27 M	130/78		0 26	0 25
8	37 M	118/80			0 05
9	24 M	114/70		0 28	0 14
10	40 M	120/86			0 09
11	42 F	75/42		0 09	
12	26 F	110/62	70/40	0 139	
13	28 F	108/56	80/50	0 315	
14	48 F	144/92	100/52	0 302 L	0 14 R
15	39 F	108/70	80/40 L	0 06 L	0 05 R
16		110/60			0 11
17		120/74 R	100/52 3 R	0 34 3 R	
		120/70 L	102/54 3 L	0 36 3 L	
18		112/70			0 05
19		98/62		0 25 3 L	0 19 R
		98/64			
20		100/64	90/55	0 13 2 R	0 10 R
		100/64			
21		100/60	88/32 L	0 32 4 L	
			70/38 R	0 34 4 R	
22	39 M	112/78	90/64	0 20 2 L	
23	35 F	100/70	90/50	0 27 4 R	
24	40 M	108/70	85/?	0 32 4 R	

of the disease[11, 125, 380] Since sympathectomy however is often incomplete and furthermore may defeat its purpose by increasing intrinsic resistance (p 139)[414] it is not unusual for the effects of the operation to be temporary[401] In addition *digital syncope may occur after sympathectomy* because of circulating norepinephrine[153, 534] and by virtue of the direct effect of cold on digital arteries[186, 347]

Emotional readjustment and warmth in the form of clothing especially gloves and stockings heating of conveyances offices factories and homes or change of climate are of great importance in treating the Raynaud's patient[17, 401] Of the blocking drugs used priscoline appears to be currently the most popular[223] It is of the utmost importance in any patient with Raynaud's spasm to clarify the role of any underlying systemic disturbance which may be present and may require treatment[26, 401]

TABLE 19 — The Digital Circulation in Thrombophlebitis (M ndl w t ...)

Patient	Age and Sex	After indirect heating and TEAC (5 mg/kg)			
		Brachial B P (mm Hg)	Digital B P (mm Hg)	Digital Blood Flow (calorimetric) (cc/cm²/min)	
				Finger	Great toe
1	32 M	120/82		0 13	
2	32 M	128/88	64/54 F	0 15	
3	25 M	120/64			0 21
4	38 M	110/70			0 05
5	38 M	122/88		0 33	0 16
6	28 M	120/70			0 19
	32 M	20/60			0 16
8	29 F	96/68			0 22
9	M	130/94			0 20
10	38 M	122/88	92/74 F	0 339	
11	31 M	32/88	120/? GT		0 24
12	M	120/ 4	4?/? GT		0 33
13	53 M	112/ 0	90/? GT		0 16
14	35 M	108/70	80/? GT		0 14

THROMBOPHLEBITIS AND LYMPHEDEMA

Although acute phlebitis may produce reflex increase in flow,[244] chronic venous obstruction rarely if ever produces a detectable decrease *in digital* blood flow when measured *after* inhibition of sympathetic nerve discharge [11, 404] In our experience in addition edema associated with local venous obstruction *is rarely* caused by the obstruction itself but rather by associated lymphatic obstruction [401] This is evident *by the usual failure* to find increased venous pressure in the obstructed vascular bed [411] It would *therefore* seem that most local obstructive edema is actually lymphedema Even in these cases we *were unable* to find any evidence of decreased blood flow or increased resistance after inhibition of sympathetic nerve discharge[401] (tables 1 and 19) Unless the edema is extreme therefore it probably has *little if* any fundamental effect on the digital circulation [11] Finding decreased blood flow *or* increased resistance in such cases must therefore always suggest *associated* arterial obstructive disease [411]

ARTERIOSCLEROSIS

Arteriosclerosis is often seen *in* both upper and lower extremities in the elderly patient although probably more often in the lower [17] Extensive calcification of these vessels may be seen without any evidence of vascular narrowing or arterial insufficiency [17] It must be remembered however that arterial insufficiency does not *occur under* ordinary circumstances unless the degree of vascular narrowing is extreme [17, 401] Preliminary studies in various age groups suggest that the factor of age alone including

TABLE 20 A — *Cont of Subjects (Mendlowitz Grossman and Alpert*[408]*)*

Case no	Age	Blood flow toe (cc / cm m n)	Date of test	Case no	Age	Blood flow toe (cc / cm m n)	Date of t t
1	39	0 23	3-4-52	16	29	0 15	6-17 49
		0 22	3-12-52			0 23	6-17 49
2	34	0 25	3-11-52	17	22	0 21	1-12 50
		0 28	3-19-52			0 22	1-17 50
3	31	0 17	5 12-50			0 28	4-20-50
		0 10	2-19-52	18	46	0 17	3-6-52
		0 16	3 10-52			0 12	3-18 52
4	32	0 18	3-7-52			0 18	4-4 52
		0 21	3-18-52	19	22	0 19	1-18-52
5	34	0 17	3-6-52			0 18	3-7-52
		0 22	3-25-52	20	44	0 21	2-21-52
6	32	0 17	8-11-49			0 15	3-5-52
		0 13	2-8-52	21	28	0 12	3-4 52
		0 20	4-4-52			0 15	3-5-52
7	41	0 23	6-6-49	22	41	0 15	2-7-52
		0 19	2- -52			0 27	2-8-52
8	30	0 29	10-19-49	23	45	0 16	1-29 52
		0 23	12-20-51			0 16	1-30 52
9	44	0 24	10-21-49	24	26	0 14	1-5 50
		0 11	10-9-51			0 20	1-26 52
		0 21	12-7-51	25	46	0 17	1-22 52
10	34	0 20	8 18-49			0 21	1-23 52
		0 25	10-25-51	26	23	0 1	1 11 52
11	41	0 26	11-2-49			0 1	1-15 52
		0 22	10-23-51	27	17	0 25	10- 49
12	32	0 24	6-27-49			0 27	1-10 52
		0 22	10-18-51	28	25	0 25	1-29 52
13	30	0 21	3 14-52			0 2	4 1 52
		0 21	3-17 52	29	45	0 32	12 31 51
14	38	0 27	11-3 49			0 28	3 24 52
		0 23	10-17-51	30	31	0 20	1 24 52
15	45	0 19	12-2 49			0 24	3 26 52
		0 24	10-16-51				

the development of arteriosclerosis produces gradual narrowing of the arterial channels over the years [401] although only in certain cases to the point of arterial insufficiency The involvement of the intima relative to that of the media may be one of the determining factors in this process This change with age however has not yet been thoroughly explored statistically

At any point in the development of arteriosclerosis one may be faced with occlusion of arterial channels the most common cause of which is thrombosis [17 401] Thrombosis may occur in the larger as well as in the smaller arteries and may recur in collateral channels until the reduction of circulation is sufficient to produce intermittent claudication and finally gangrene [17 401]

TAB E 10 B—*C ntrol Subjects (Mendlowitz Gr ssman and Alpert* [*])

Case	Ch lesterol (mg /100 cc.)	Phosph l p l (mg P/100 cc)	Ch leste l phosphol p d rat $\left(\frac{C}{25\ P}\right)$
1	210	8 8	0 95
2	230	9 1	1 01
3	157	10 2	0 68
4	184	9 0	0 82
5	186	8 7	0 86
6	178	9 6	0 74
7	218	9 5	0 90
8	256	8 2	1 25
9	288	9 4	1 23
10	270	13 2	0 82
11	310	13 5	0 92
12	173	6 4	1 08
13	242	10 2	0 95
14	230	13 9	0 66
15	200	13 9	0 58
16	194	9 3	1 26
17	310	14 1	0 80
18	242	8 8	1 10
9	302	10 3	1 17
20	236	9 6	0 98
21	288	7 20	1 60
2	310	10 6	1 17
23	194	7 30	1 06
24	224	8 62	1 04
5	204	9 34	0 87
26	188	10 5	0 70
2	242	3 2	0 73
8	348	2 8	1 09
9	270	11 8	0 88
30	320	16 8	0 6

Occlusive arteriosclerotic thrombosis differs very little from that occurring in thromboangiitis obliterans except for the occasional con comitant occurrence of superficial venous thrombosis in the latter dis ease [401] [404] In fact it might be wiser to speak only of arterial thrombosis migrating venous thrombosis[183] and arteriosclerosis as separate conditions occurring either individually or in combination without attempting to establish rigid clinical compartments [401]

Three conditions which favor the development of arteriosclerosis are hypertension [167] diabetes[131] [12] [6 0] and probably hypercholesterolemia [417] In recent studies[240] [387] [405] [408] it has been shown that one of the earliest manifestations of vascular disease in diabetes is obstruction of the small arterial channels in the foot Arteriosclerosis in other regions involving the larger vessels is a later phenomenon [405] [406] Hypertension also pro duces arteriolosclerosis with narrowing of the small blood vessels through

TABLE 20 C.—*Uncomplicated Diabetes (Mendlowitz, Grossman and Alpert*[406]*)*

Case no	Age	Year of onset	Insulin dosage	Degree of control	Cholesterol (mg /100 cc)	Phospholipid (mg P/100 cc)	C P ratio $\left(\frac{C}{25 P}\right)$	Blood flow toe (cc / cm min)	Date of test
1	42	1949	NPH 10	Good	254	8 9	1 1	0 16	1-13-50
								0 18	3 1-50
2	44	1945	NPH 44	Good	301	10 35	1 05	0 19	12-1-49
			R 4					0 13	12-21-50
								0 22	8-14-51
3	40	1945	NPH 48	Poor	260	11 2	0 93	0 14	12-1-50
			R 5					0 12	3 6-51
4	33	1945	PZI 70	Poor	227	7 6	1 2	0 15	1-6-50
								0 21	11-30-50
5	46	1944	NPH 60	Fair	157	7 0	0 90	0 24	11-2-50
								0 21	6-29-51
6	34	1943	NPH 50	Poor	222	10 3	0 80	0 10	12-5-49
								0 21	5-2-51
								0 17	8 22-51
7	30	1946	NPH 55	Poor	328	8 7	1 5	0 24	10-16-50
			R 10					0 12	3-19-51
								0 22	7-23-51
8	38	1945	PZI 36	Fair	310	9 0	1 38	0 24	11-7-50
								0 28	5-7-51
9	43	1945	NPH 45	Poor	358	15 2	0 94	0 12	8-21-51
								0 09	1-8-52
10	32	1945	PZI 68	Fair	194	8 2	0 95	0 15	12-20-50
								0 25	5-26-51
11	35	1946	NPH 68	Fair	283	11 6	0 97	0 03	1-16-50
								0 06	2-3 50
12	34	1946	0	Fair	265	10 0	1 06	0 17	1-18 50
								0 28	8-17 51
13	46	1944	NPH 42	Fair	194	9 2	0 84	0 25	12-25-49
								0 27	10-5 50
14	34	1945	NPH 50	Fair				0 19	12-5 49
								0 15	10-23-50
15	27	1946	NPH 60	Poor	270	12 8	0 84	0 21	1 27 50
								0 19	9-18 51
16	34	1945	NPH 80	Poor				0 21	10-16 50
								0 20	10-13 51
17	36	1943	PZI 18	Fair	184	7 42	0 99	0 13	11-14 50
			R 24					0 18	8 16-51
								0 12	2 15 52
18	41	1948	NPH 68	Poor	185	8 3	0 89	0 24	12-13 49
								0 32	10-25 50
19	25	1946	NPH 55	Poor	264	10 9	0 97	0 22	12 16 49
								0 21	7 13 51
20	28	1946	NPH 65	Poor	196	8 0	0 98	0 21	1 3 50
								0 20	11 8 50
21	31	1947	0	Good				0 08	1 12 51
								0 20	7-31 51
22	30	1946	NPH 65	Poor	264	9 5	1 11	0 15	10-3-50
								0 17	2-4-52
23	40	1946	NPH 35	Good	260	12 9	0 80	0 05	12 13 50
								0 08	5 29-51

TABLE 20 C.—C n d

C se n	Ag	Yea f set	I l dosag	Degree f c t l	Ch l t l (mg 100 c)	Phosp ho- l p d (mg P /100 c)	C P ratio $\left(\frac{C}{2\ P}\right)$	Bl od flow toe (/ cm m)	D te f test
24	28	1948	PZI 1 R 34	Fair	230	9 35	0 99	0 25 0 22	12 29 49 4 11 51
25	35	1945	PZI 48	Fa r	248	10 0	1 0	0 0 0 0	12 29 49 3 6 51
26	41	1944	PZI ,0	Fair	228	8 9	1 02	0 25 0 19	11 2 50 6-12 51
2,	42	1945	NPH 68	Poor	298	12 0	0 99	0 16 0 14	11 25 49 10-5 50
28	5	1946	PZI 30 R 45	Good	189	9 3	0 81	0 09 0 13	2 2 51 3 9 51
29	43	945	NPH 15	Good	260	10 4	1 0	0 06 0 11	1 20 50 8 31 51
30	35	946	NPH 68	F r	242	8 8	1 1	0 09 0 19 0 13	5 14 51 9 4 51 2-18 52
31	3	946	NPH 50	P or	234	10 6	0 90	0 19 0 24	1 17 50 10-4 50
3	54	1943	0	Good	234	9 3	1 0	0 15 0 17	1 12 50 5 29 51
33	44	945	NPH 70	Poor		12 0		0 13 0 10	10-5 50 3 14 51
34	24	1947	PZI 2 R 24	Fair	216	9 03	0 96	0 09 0 05	12 5 50 7 18 51
35	31	1944	PZI 40 R 56	Poo	314	11 1	1 13	0 24 0 13 0 24	10-11 50 3 9 51 2 12 52
36	30	1945	NPH 68 R 0	Poor	352	12 5	1 11	0 18 0 21	1 16 50 12 6 50
37	36	946	NPH 100	Poor	230	8 2	1 12	0 25 0 23	12 22 49 11-17-50
38	29	944	NPH 70	Fa	240	9 48	1 01	0 08 0 19 0 24	1 13-50 10-24 50 10-16 51

out the body including the digits [157, 395, 399] Sclerosis of the larger blood vessels is again a later effect [157] Obliterating thrombotic arterial disease is often the complication which produces vascular insufficiency in the lower extremities [401] Such insufficiency may however be caused by arterio sclerosis or arteriolosclerosis itself [17, 401] Table 20 and figure 51 A and B illustrate findings in diabetes [401, 40, 406] and in arteriosclerosis involving the lower extremities

As with other occlusive diseases of the arteries arteriosclerosis and arteriolosclerosis produce increased resistance and decreased flow after in hibition of sympathetic nerve discharge [401, 404] Blood pressure is increased if the process in the arterioles is sufficiently widespread [399] Thrombotic occlusion of larger vessels on the other hand produces increased brachial

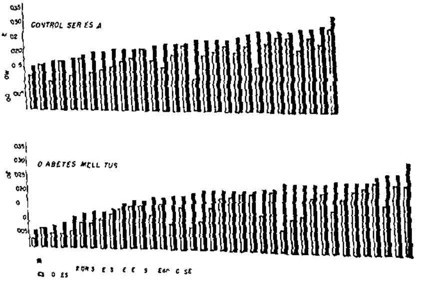
TABLE 10 D.—*Statistical Analysis (Mendlowitz, Grossman and Alpert[106])*

Group	No. of cases	Determination	Range	Mean	Standard deviation	Standard error of the mean	Difference between the means	Standard error of the difference between the means	Probability that difference is due to chance
Control Series A	30	(1) Lowest blood flow in each patient (cc./cm.²/min.)	0.10–0.28	0.185	0.046	0.0083 }	0.045	0.0112	0.00006
		(2) Highest blood flow in each patient (cc./cm.²/min.)	0.15–0.32	0.230	0.041	0.0075 }			
		(3) Average of all blood flows in each patient (cc./cm.²/min.)	0.13–0.30	0.208	0.040	0.0073			
Diabetes	38	(4) Lowest blood flow in each patient (cc./cm.²/min.)	0.03–0.25	0.146	0.058	0.0095 }	0.049	0.0139	0.0005
		(5) Highest blood flow in each patient (cc./cm.²/min.)	0.06–0.32	0.195	0.062	0.0075 }			
		(6) Average of all blood flows in each patient (cc./cm.²/min.)	0.05–0.28	0.170	0.058	0.0093			
		(1) & (4)					0.039	0.0126	0.002
		(2) & (5)					0.035	0.0126	0.005
		(3) & (6)					0.038	0.0118	0.002
Control Series B	30	(7) Cholesterol (mg./100 cc.)	157–348	243.50	51.4	9.40			
		(8) Phospholipid (mg. P/100 cc.)	6.4–16.8	10.50	2.4	0.44			
		(9) Cholesterol Phospholipid ratio (C/25 P)	0.66–1.60	0.96	0.22	0.04			
Diabetes	38	(10) Cholesterol (mg./100 cc.)	157–358	250.0	48.90	8.15			
		(11) Phospholipid (mg. P/100 cc.)	7.0–15.2	9.94	1.78	0.301			
		(12) Cholesterol-Phospholipid ratio (C/25 P)	0.80–1.50	1.02	0.1384	0.0230			
		(7) & (10)					7.2	12.42	Greater than 0.5
		(8) & (11)					0.52	0.53	0.31
		(9) & (12)					0.065	0.0464	0.16

TA LE 20 E —*The Digit l Circulati n in Arteri sclerosis* (*Men l* au tr ¹)

P t t	Age nd se	Aft r ind rect heat g a d TEAC (3 mg /Kg)	
		Bra hi l B P (mm Hg)	D g blood flow l k j m t c (cc m m n) Gr t toe
1	34 M	118/90	0 21
2	52 M	110/84	0 01
3	42 M	100/68	0 10
4	36 M	110/88	0 16
5	66 M	116/78	0 05 L
			0 04 R
6	59 M	128/88	0 054
7	61 M	126/82	0 095 L
			0 038 R
8	65 M	120/ 8	0 01

digital pressure gradient [274] and decreased digital pressure and flow,[315] without necessarily affecting the resistance In the larger blood vessels decreased elasticity produces increased pulse pressure decreased pulse wave velocity and decrease in the height or even disappearance of the dicro ic w ave (fig 51 C) [337] whereas in the smaller vessels pulsations are usually decreased because of obstruction[247 579] and the histamine flare is diminished or absent [545] Intermittent venous congestion[104] has been demonstrated to have no therapeutic effect in the treatment of occlusive



F 5 A top) nd B (bott m) —Blood flow i pati nts w th uncompl c ted diabetes of le s than 1 ye rs d ation with no other manifestat ons of scular d se se compared with a control g oup (Mendl wit Gro m and Alpert ⁴ courte sy Am J Med)

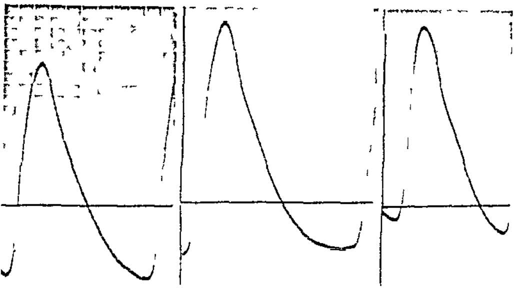


FIG 51 C — Pulse wave recordings obtained from the digit of patients with arteriosclerosis showing absence of a dicrotic wave (Lax and Feinberg [337] reproduced with authors permission)

arterial disease[178] and sympathectomy has little or at most a transient, effect on the process Intra-arterial injection of vasodilator drugs such as histamine or priscoline combined with antibiotics appears currently to be promising [4 9]

TRENCH FOOT AND FROSTBITE

Trench foot was first described in 1812 by Napoleon s Surgeon General Baron D J Larrey [335] in soldiers returning from the Russian campaign Since that time the subject has been of increasing importance in military naval and also civilian medicine [53] Numerous clinical and pathologic [57, 178, 313, 349, 580, 597, 605, 606, 6 9] as well as some experimental investigations[133, 451] have been carried out It is generally agreed that immersion foot trench foot chilblains [349] erythrocyanosis [349, 570] and Bazin s disease[41, 383, 4 1] are similar pathologically whereas frostbite belongs in a different category and is due to actual freezing of tissues In some cases however, it is possible for frostbite and trench foot to occur together and when gangrene supervenes in trench foot the pathologic changes may be difficult to distinguish from those of severe frostbite

In trench foot (fig 52) the injury seems to involve chiefly nerve and muscle tissue [60] Tight shoes and socks and lack of exercise are contributory factors [448] The blood vessels are affected only in that their permeability is increased the reaction being that of aseptic inflammation [81] When the skin is broken secondary bacterial infection may supervene [178] *Thromboses in major vessels including arteries appear to occur as* secondary phenomena in the wake of gangrene [178a]



FIG 52 —Trench Foot (left) Hemorrhage cyanosis and edema of the foot 5 days after exposure The sharp line separating the involved from the normal tissues is evident This is typical of the early change observed in trench foot Dry gangrene of the toes in a case of severe trench foot seventeen days after exposure (middle and right) The toes later sloughed (Friedman courtesy Am J Path)

In frostbite (fig 50) on the other hand if the process is sufficiently prolonged the increased permeability of the small vessels together with extreme vasoconstriction [109] causes loss of plasma from the vessels with a remaining obstructive sludge of red cells [126] These cells may be swept into the veins when the circulation reopens or may be fixed sufficiently to produce permanent obstruction It is believed by some[122, 124] and denied by others[4, 2] that this vascular obstruction can be prevented by the timely administration of heparin When frostbite produces gangrene fibrinous thrombosis may occur secondarily as in trench foot [128]

A physiologic approach to the study of trench foot was made in 1945 by Schechter and Ragan[503] who used ischemic pain as an index of the severity of the injury In 1946 Paddock[481] studied patients one to two years after their recovery from trench foot and found evidence of persistent nerve and muscle lesions as manifested by sensory changes and muscular weakness He also measured skin temperatures and noted color changes after the production of hyperemia by the application of direct and indirect heat but could find no evidence of vascular obstruction in most of his patients In 1947 Burch Myers Porter and Schaffer[81] reported extensive physiologic studies designed to determine whether the presence of low grade inflammation could be demonstrated in patients with trench foot They measured the degree of reactive hyperemia under exacting conditions of room temperature and covering after a fixed period of vascular occlusion of the leg with a pressure cuff and attempted to classify their patients on the basis of these reactions

Mendlowitz and Abel studied blood flow after inhibition of sympathetic nerve discharge as measured calorimetrically in a group of patients and normal subjects [40] They found blood flow values below the lower limit of normal in about 25 per cent of the former (table 21)

The decreased blood flow observed in these patients might be attributed to failure to achieve maximal vasodilatation because of persistent nerve lesions [40] However, in the patients reported here, demonstrable sensory and motor nerve lesions were absent It is more likely, therefore, that the diminished blood flow represents actual obstruction of the small arterial channels of the foot [40] This obstruction may be due to initial occlusion of blood vessels by sludge as in frostbite,[1, 6] to secondary thromboses,[178] or to the contraction of perivascular scar tissue [60] In treating the acute manifestations of cold injury, rapid rewarming appears to be most satisfactory provided care is taken not to apply heat above 37 C directly to the involved tissues Warming by indirect heat is more desirable [50] Amputation may be necessary, although if gangrene is superficial healing can often take place satisfactorily [50] Nerve block and sympathectomy have been recommended for late therapy especially if a large vasospastic factor can be demonstrated [520] Intra arterial histamine might also be useful [50]

TABLE 21 A —*Normal subjects (Mendlowitz and Abel[102])*

Patient	Test no	Age in years	Sex	Blood flow (toe) (cc/m/cm m)	Digital blood pressure (systolic) (mm Hg)
1		35	M	0.18	72
2		41	M	0.15	112
3		21	M	0.24	101
4		24	M	0.25	95
5		28	M	0.15	82
6		24	F	0.20	88
7		24	M	0.26	92
8		26	M	0.16	92
9		21	M	0.16	84
10		38	M	0.23	102
11		38	M	0.16	104
12		24	M	0.20	98
13		40	M	0.14	78
14		40	M	0.16	92
15		32	M	0.21	78
16		30	M	0.16	65
17		32	M	0.14	78
18	1	36	M	0.10	108
	2			0.15	90
19		27	M	0.27	60
20		31	M	0.18	64
21		32	M	0.23	60
22		31	M	0.19	90
23		28	M	0.17	88

TABLE 21 B — *Patie ts ith Re idual Sympt ms of Trench Fo t and Frost Bite (Mendlowitz and Abel* [11])

P t t	Test o	Ag I y ars	Sex	Blood flow (toe) (Gm / m m)	D g t l blood P es ure (y t l) (mm Hg)
1		23	M	0 20	90
2		28	M	0 18	96
3		22	M	0 14	80
4		26	M	0 13	58
5		23	M	0 11	68
6		22	M	0 13	86
		31	M	0 16	88
8		25	M	0 14	84
9		22	M	0 15	88
10		24	M	0 15	86
11	1	25	M	0 09	60
	2			0 16	60
12	1	35	M	0 11	60
	2			0 11	60
	3			0 11 left	60
				0 11 right	74
13	1	23	M	0 03	-0
	2			0 02	90
14		23	M	0 14	98
15		22	M	0 08	8
16	1	32	M	0 0	86
	2			0 10	96
7		33	M	0 15	6
8		28	M	0 14	90
9		34	M	0 17	8
20		29	M	0 11	110
2	1	29	M	0 11	90
	2			0 11	78
22		21	M	0 24	102
23	1	32	M	0 10	94
	2			0 06	90
4		21	M	0 18	-8
25	1	23	M	0 13	84
	2			0 21	74
6		35	M	0 06	90
				0 21 left	88
				0 20 right	88
2		34	M	0 20 left	90
				0 23 right	84
28		30	M	0 19	102
29		23	M	0 17	118
3		26	M	0 20	98
31		24	M	0 15	90
3		38	M	0 23	98
33		33	M	0 17	72
34		30	M	0 21	114
35		32	M	0 15	70
36		33	M	0 15	70
3		22	M	0 19	74
38	1	32	M	0 11	100
	2			0 15	84
39		39	M	0 7 left	78
				0 11 right	61
	2			0 13 right	58
4		36	M	0 18	94

NEUROGENIC ACRAL VASOSPASM (ACROCYANOSIS) AND LIVEDO RETICULARIS

The most common cause of acrocyanosis is vasospasm of arterioles and arteriovenous anastomoses due to increased sympathetic nerve tone[353] The cyanosis is produced by the greater extraction of oxygen from the slowly moving blood An additional factor is loss of capillary[60] and venular[146] tone Acrocyanosis is therefore a descriptive term[3] of dubious usefulness and should be replaced by the expression neurogenic acral vasospasm[401]

Although usually vasospastic the cyanosis itself may be produced by any type of pathologic vascular obstruction or by any systemic condition producing increased amounts of reduced hemoglobin in the arterial blood In the latter instance the cyanosis may be more marked acrally because of associated vasospasm[401]

Acrocyanosis is also seen as a feature of cold injury as well as in Raynaud s disease[401] Here the question of which condition is cause and which effect often arises In fact there may possibly be a variable cyclic arrangement of cause and effect in these conditions[401] Acrocyanosis is less pronounced in the presence of hypertension, the latter tending to produce more normal circulation despite vasospasm[401] Patients with acrocyanosis are often poorly adjusted socially The cold blue clammy hand accentuates social maladjustment which is one of its causes by repelling social intercourse[401] Sexual frustration sometimes with resultant perversion is a not infrequent feature of this condition[401] Structurally there is no impairment in the digital circulation as can be demonstrated after inhibition of

TABLE 22 —*The Digital Circulation in Neurogenic Acral Vasospasm (Acrocyanosis) (Mendlowitz[401])*

Patient	Age and sex	After indirect heating and TEAC (5 mg/Kg)			
		Brachial B P	Digital B P	Dig blood flow (calorimetric) (cc/cm/min)	
				Finger	Great toe
1	21 M	148/88		0 2, L 0 28 R	
2	30 M	110/68			0 17
3	27 M	120/70	88/68	0 27	
4	37 M	128/,8			0 16
5	36 M	100/62		0 32 L 0 34 R	
6	29 M	118/65	74/?	0 334 L	
7	19 M	120/88	92/? 100/54	0 373 L	0 23 L
8	30 M	112/86	82/? 88/64	0 433 R	0 31 R
9	39 M	130/90	90/?		0 11

sympathetic nerve discharge by indirect heating supplemented by blocking drugs (table 22) [401-404]

Livedo reticularis is usually seen in the proximal part of the extremity rather than the digits [8, 17] It is a reticulated vasodilatation often bluish and sometimes seen together with acrocyanosis [17] Blood flow in the digits after inhibition of sympathetic nerve discharge is usually normal [401, 404] The pattern is produced by the tufted arrangement of the arteriolar bed the reticulations being caused by slower flow and greater extraction of oxygen at the edges of these tufts [8] In children it is often physiologic and is accentuated by cold vasoconstriction [17] Permanent livedo may be caused by venous obstruction or by any mild vasculitis such as is produced by cold[8] or radiant heat [8] especially in anatomically susceptible individuals Skin biopsy may be confusing and may reveal perivascular round cell infiltrations and thrombosis suggestive of other more generalized diseases [114] In severe cases there may be secondary ulcerations[118] and the reticulations may determine the site of the development of other skin diseases [38, 619]

ERYTHROMELALGIA AND CAUSALGIA

Although a rare idiopathic form probably representing a hyperemic reaction to known or unknown dermal irritation [17, 401] is believed to occur, erythromelalgia[98, 416, 417] is most often caused by occlusive disease of the peripheral arteries [17, 401] Ischemic necrosis and reactive hyperemia are responsible for the pain and redness [315] Digital circulation after inhibition of sympathetic nerve discharge is usually very low [401]

So-called causalgia on the other hand is a severely painful state usually brought on in an extremity and especially in the digits by a relatively minor injury [76] The term is probably a catch all including various pathologic states such as *neuromas* glomus tumors and others [401] Some psychoneuroses and traumatic neuroses *involving* pensions compensation or litigation are often grouped under *this rather* vague *term* [401] The sympathetic nervous system is implicated in causalgia [1, 8, 449] either because of imbalance between sympathetic nerve vasomotor tone and tissue need or a connection between sympathetic and sensory nerve function [401] In such cases sympathetic block is effective therapy and sympathectomy may be indicated [401]

7

CLUBBING

It has been demonstrated by Mendlowitz[389, 391] and by Wilson[6 b] that acquired symmetrical clubbing of the fingers and toes is usually associated with an increase in blood flow in the fingertips This is usually caused by an increase in the arterial pressure in the digital arteries the brachial arterial pressure being unaffected [389, 390] There is therefore, a decrease in the brachial digital arterial pressure gradient It is necessary that the clubbing be advancing for these changes to be demonstrable [390, 391] When it recedes because of cure or regression of the underlying disease, the blood flow and digital pressure will also decrease, often to normal levels (table 23) [390, 62 b]

The clubbing itself consists largely of hypertrophy and hyperplasia and possibly some congestion and edema of the soft tissues of the finger tip including the nailbed [365, 366, 401] The increase in blood flow is out of proportion to the increase in tissue and can be shown to be greater than normal per unit of volume or surface of fingertip [389, 390, 6 2b] To demonstrate these changes in flow as well as pressure it is necessary to stabilize the circulation by indirect heating thus inhibiting sympathetic nerve discharge [389, 390, 622b]

Hypertrophic osteoarthropathy[373, 586, 587] is an extension of the process of clubbing to more proximal tissues [574] especially the periosteum of long bones [3 1, 391] It can be shown that blood flow per unit of tissue in the fingertip and digital arterial pressure usually become normal with the development of hypertrophic osteoarthropathy [390] This is probably caused by the tapping off of sufficient blood by the bones to decrease digital arterial pressure and flow and stabilize the clubbing at a certain level [390, 401] In hypertrophic osteoarthropathy produced in dogs by anastomosing the

pulmonary artery to the left auricle, there is a pronounced increase in systemic cardiac output (figs 53 and 54 table 24) [407, 409]

In hereditary clubbing [129, 169, 174, 74, 265, 310] both the digital pressure and the flow per unit of tissue after indirect heating are normal [389, 390] This does not preclude the possibility that the initiating factor in hereditary clubbing may be increased circulation which subsequently becomes stabilized and ceases to cause the clubbing to advance [391, 401] Whether this is attributable to an early defect in sympathetic innervation or to some systemic abnormality which becomes corrected is conjectural since in the resting state plethysmographic pulsations seem to be slightly decreased [379] Occasionally hereditary clubbing advances in middle life and in one such case this advance was associated with hypertension [391] If such a relationship can be corroborated it may lend weight to the theory of a local defect in sympathetic innervation as the initiating cause of hereditary clubbing [391, 401]

Unilateral [389, 391] and unidigital [442] clubbing often present complicated problems difficult to analyze which may however at times throw light on the mechanism of clubbing [391] It is for example well established that unidigital clubbing may occur after injury especially to a nerve [442] and

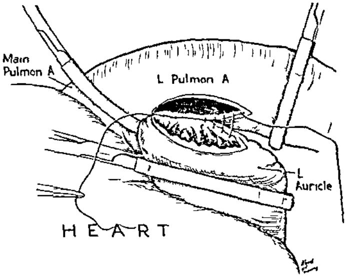
TABLE 23 A.—*The Digital Circulation in Normal Subjects and in Patients with Various Chronic Diseases After Release of Sympathetic Nerve Tone by Indirect Heating (Mendlowitz)*

Diagnosis	Blood flow (cc/cm³/min)	Brachial arterial pressure (mm Hg)	Digital arterial pressure (mm Hg)	Arithmetic mean gradient (mm Hg)
Normal	0.28	128/80	120/70	9
Normal	0.17	102/74	88/40	24
Normal	0.24	125/84	96/52	30
Normal	0.31	135/94	110/76	21
Normal	0.26	114/82	106/52	19
Normal	0.31	132/86	116/60	21
Normal	0.30	1[illegible]2/82	84/70	20
Normal	0.31	1[illegible]8/80	102/67	23
Normal	0.26	118/85	102/64	18
Normal	0.32	118/90	96/60	26
Normal	0.29	116/86	98/54	25
Aplastic anemia	0.23	124/90	100/35	40
Hyperthyroidism	0.[illegible]2	112/70	96/64	11
Hypertension	0.24	13[illegible]/78	100/84	12
Acromegaly	0.22	[illegible]38/125	216/[illegible]30	9
Acromegaly	0.24	108/86	104/?	
Rheumatoid arthritis	0.[illegible]3	120/78	108/64	13
Rheumatoid arthritis	0.[illegible]3	120/80	100/76	12
Chronic pyelonephritis	0.29	106/74	90/74	8
Chronic pyelonephritis	0.27	186/92	142/98	2
Tuberculous nephritis	0.32	140/82	1[illegible]8/64	15
Chronic salpingitis	0.27	128/38	108/70	24
[illegible]	0.26	[illegible]	[illegible]	[illegible]

TABLE 23 B—*The Digital Circulation in Patients with Clubbed Fingers After Release of Sympathetic Nerve Tone by Indirect Heating (Mendlowitz[390])*

Diagnosis	Blood flow	Brachial arterial pressure (mm Hg)	Digital arterial pressure (mm Hg)	Arithmetic mean gradient
Bronchiectasis	0 36	104/74	104/58	8
Bronchiectasis	0 41	136/92	128/94	3
Bronchiectasis	0 36	128/90	122/74	11
Bronchiectasis	0 38	142/90	126/80	13
Bronchiectasis	0 36	136/90	124/76	13
Bronchiectasis	0 33	124/84	120/70	9
Bronchiectasis	0 41	136/70	134/?	
Bronchiectasis	0 38	112/74	106/65	7
Lung abscess	0 38	125/74	116/66	9
Lung abscess	0 27	126/98	102/82	20
Lung abscess				
(Preoperative)	0 36	138/82	110/80	12
(Postoperative)	0 30	112/75	90/68	15
Empyema	0 32	138/80	124/72	11
Pulmonary tuberculosis	0 34	112/80	108/74	5
Pulmonary neoplasm	0 29	124/78	128/72	1
Congenital heart disease	0 32	112/94	108/75	11
Congenital heart disease	0 34	102/88	92/66	16
Subacute bacterial endocarditis	0 54	130/?	128/?	
Subacute bacterial endocarditis	0 36	110/55	105/55	3
Subacute bacterial endocarditis	0 38	90/75	84/74	4
Subacute bacterial endocarditis	0 37	124/75	110/66	12
Subacute bacterial endocarditis	0 34	102/65	86/62	9
Subacute bacterial endocarditis	0 32	12-/74	96/64	16
Subacute bacterial endocarditis	0 32	104/72	102/?	
Ulcerative colitis	0 30	96/60	94/?	
Ulcerative colitis	0 36	120/86	118/84	3
Ulcerative colitis	0 33	114/80	110/74	5
Chronic dysentery	0 27	110/85	98/82	7
Regional ileitis	0 36	102/64	10-/60	2
Sprue	0 38	138/102	116/?	
Sprue	0 23	84/56	76/?	
Osteoarthropathy (empyema)	0 28	124/68	95/65	16
Osteoarthropathy (pulmonary neoplasm)	0 32	132/85	126/?	
Osteoarthropathy (pulmonary neoplasm)	0 26	92/66	82/?	
Hereditary clubbing	0 30	145/95	125/84	16
Hereditary clubbing				
(Clubbed finger)	0 24	126/78	104/58	21
(Normal finger)	0 24	126/78	108/64	16

presumably to sympathetic nerves[401] The effect of such injury is to decrease sympathetic vasomotor tone and hence increase blood flow in the affected finger (fig 55)[401] In one case the clubbing was complicated by disuse atrophy[401] Peripheral neuroma[379] and also apical tuberculosis[446] as well as apical tumors of the lung[391] by destruction of the sympathetic nerves on the affected side may increase clubbing presumably because



F c 53A —Anatomic relationsh p in detail of suture anastomoses resulting in hypertrophi o te r-rthropathy in dog (Mendlowitz and Leslie [97] courtesy Am Heart J)



F G 53B —The heart f the d g how ng open r ght entricle and p lmonary rtery RP = r ght pul m a y artery or fic P = left pulm n y artery ope ed A = pulmonary a tery or fice of ana tomosis to l ft a ricle (Mendl w tz d Le l e [97] co tesy Am Heart J)



FIG 53 C —Cyanosis was produced in a dog on left by anastomosis of left pulmonary artery to the left auricle The dog on the right is normal (Mendlowitz and Leslie [407] courtesy Am Heart J)

vasomotor tone is less and blood flow therefore greater on the involved side The subsequent moderation of this process is described elsewhere (p 139) [414] Clubbing can also be decreased unilaterally in congenital heart disease (table 25) by anastomosis of the subclavian to the pulmonary artery [401, 6, 2b]

Unilateral clubbing (fig 56) [24, 362] is usually however produced by brachial,[391] axillary [18] innominate [41, 49] or subclavian arterial aneurysm [47, 138, 164, 467] and is often complicated by intra arterial thrombosis venous obstruction and thrombosis and sympathetic nerve irritation as well as destruction by pressure and by sensory and motor nerve pressure effects [391, 6, 2b] If a case is seen sufficiently early however increased blood flow and pressure can be demonstrated in the digits on the involved side [119, 389, 6, b] Unilateral clubbing is also seen in so called cirsoid aneurysms of the extremity [389, 540] many of which may actually represent arteriovenous aneurysms incurred at birth or within the womb The complicating factors here are so difficult to unravel and the cases so rare that no conclusions can be drawn as to the mechanism of the clubbing (table 26) In acquired [70, 71] or congenital[367] arteriovenous fistula there may be increased growth of the entire extremity distal to the fistula rather than simple clubbing This may be associated with increased pressure and flow in the region involved [6]

It might be pertinent here to discuss the mechanism of clubbing and





Fig 54A (left)—Comp ri on of uln of dog (left) with hypertr pl ic o te arthr pathy produced experime t ll with ul a of normal dog (right)

Fig 54B (right)—Photomicrograph of trans erse sectio n of tibia of d g with hypertrophi osteo-arthropathy prod ced exper m nt lly Arro points to new normal peri steal bone (Both figure from Mendlo t nd Leslie courtesy Am Hea t J)

present what appears to be the most reasonable theory at the present time It has been demon trated pathologically that hypertrophy and hyperplasia of soft tissues is indeed the most important feature of the process of club bing [365 366 391 401] Demonstration of increased vascularity and increased arterial caliber also confirms the part played by overnutrition due to increased blood supply [365] In congenital heart disease great distention of the venules can also be demonstrated although it is possible that secondary polycythemia accounts for at least part of this effect [365]

The theory that clubbing is caused by anoxemia[109] or that anoxemia is at least a factor in clubbing has had many adherents[1 7] and on the basis of speculative reasoning Mauer has readvanced this idea [377 378] He feels that since rapid sedimentation rate is associated with rouleaux formation this may occur intravascularly and that together with the sludging phe nomenon[64] it may be responsible for interfering with oxygen delivery to the tissues He accepts the view that increased peripheral circulation is also a factor This theory is inconsistent with many known facts [401] Local tissue anoxia as in occlusive peripheral arterial disease is rarely if ever associated with clubbing [391] Arterial anoxemia occurs very often without clubbing as in chronic cor pulmonale [401] Rapid sedimentation rate as in chronic osteomyelitis is rarely productive of clubbing despite frequent low

TABLE 24 —*Physiologic Data in Four Dogs Before and After Successful Anastomosis of the Left Pulmonary Artery to the Left Auricle (Mendlowitz and Leslie[40])*

Dog No	237		262				294				335	
Time	2 weeks preop	3 months postop	2 weeks preop	1 month postop	7 months postop	10 months postop	1 week preop	2 months postop	4 months postop	6 months postop	2 weeks preop	3 months postop
Weight (Kg)	17 1	17 1	20 0	19 0	22 5	22 0	19 4	18 4	18 8	20 0	15 3	14 0
Arterial blood pressure (mm Hg)	140	100	135	122	155	142	130	135	160	130	96	115
Venous pressure (cm water)	0	1 0	2 0	3 5	2 0	4 0	2 0	2 3	2 5	2 0	0	3 0
Ether time (sec)	4 0	3 0	2 5	3 5	3 0	2 5	2 5	3 0	—	4 0	—	—
Cyanide time (sec)	9 0	5 0	7 0	6 0	5 5	4 5	6 5	4 0	5 0	5 0	8 0	6 0
Blood volume (cc)	1390	1600	2579	2254	2521	2331	2139	2031	2183	2091	1825	1786
Plasma volume (cc)	750	850	1625	1375	1563	1375	1250	1300	1375	1150	1150	1000
Cell volume (cc)	640	750	954	879	958	956	869	731	808	941	675	786
Arterial blood oxygen (vol %)	22 15	16 51	16 57	16 39	16 68	15 48	19 11	12 90	17 0	17 21	15 92	17 54
Venous blood oxygen (vol %)	15 57	11 62	13 92	14 05	12 75	12 65	15 88	10 19	14 02	14 33	12 99	14 32
Saturated blood oxygen (vol %)	22 37	21 02	16 73	17 48	17 46	16 64	19 50	13 75	17 98	18 69	16 52	19 67
% saturation of arterial blood	99 0	78 3	99 0	93 7	95 5	93 0	98 0	93 8	94 5	92 1	96 5	89 2
Oxygen consumption (cc /min)	117	120	144	130	153	127	113	110	127	128	108	95
Systemic blood flow (cc / min)	1,80	2478	5420	5537	3835	4487	3500	4057	4264	4443	3696	2951
Pulmonary blood flow (cc /min)	1780	1318	5420	3987	3310	3325	3500	3343	3527	3208	3686	2039
% shunt	0	47	0	28	14	26	0	18	17	28	0	31

A op y fi d g				
	Ded 4 m h p p ll de p d pn m n a tom p t (9 mm)	D d m h p t p ll d p d p n n a na m p t t (4 mm) ped l t d th mb t di g t a r le	S c fi d 9 m h p t p Ana tomo p en d fen t t d o e pen / ng (4 mm) par ted by th n ept m f om cc d pe ng (2 n m) bpe i t l b n prol f ra ti n n l ng bones	D d 4 mo th p top Ana t mo s p tent (6 mm) p d c lat d thr m bu in auricle and thrombus p rti lly occl d ing left pulmo nary artery dis tal to anasto mosis cerebral emb lus

TABLE 24 —*Physiologic Data in Four Dogs Before and After Successful Anastomosis of the Left Pulmonary Artery to the Left Auricle (Mendlowitz and Leslie*[40] *)*

D g No	237		262				294				335	
T me	2 weeks preop	3 mo ths postop	2 weeks preop	1 month post p	7 months postop	10 months postop	1 week preop	2 months postop	4 months postop	6 months postop	2 weeks preop	3 months postop
Weight (Kg)	17 1	17 1	20 0	19 0	22 5	22 0	19 4	18 4	18 8	20 0	15 3	14 0
Arterial blood pressure (mm Hg)	140	100	135	122	155	142	130	135	160	130	96	115
Venous pressure (cm water)	0	1 0	2 0	3 5	2 0	4 0	2 0	2 3	2 5	2 0	0	3 0
Ether time (sec)	4 0	3 0	2 5	3 5	3 0	2 5	2 5	3 0	—	4 0	—	—
Cyanide time (sec)	9 0	5 0	7 0	6 0	5 5	4 5	6 5	4 0	5 0	5 0	8 0	6 0
Blood volume (cc)	1390	1600	2579	2254	2521	2331	2139	2031	2183	2091	1825	1786
Plasma volume (cc)	750	850	1625	1375	1563	1375	1250	1300	1375	1150	1150	1000
Cell volume (cc)	640	750	954	879	958	956	869	731	808	941	675	786
Arterial blood oxygen (vol %)	22 15	16 51	16 57	16 39	16 68	15 48	19 11	12 90	17 0	17 21	15 92	17 54
Venous blood oxygen (vol %)	15 57	11 62	13 92	14 05	12 75	12 65	15 88	10 19	14 02	14 33	12 99	14 32
Saturated blood oxygen (vol %)	22 37	21 02	16 73	17 48	17 46	16 64	19 50	13 75	17 98	18 69	16 52	19 67
% saturation of arterial blood	99 0	78 3	99 0	93 7	95 5	93 0	98 0	93 8	94 5	92 1	96 5	89 2
Oxygen consumption (cc /min)	117	120	144	130	153	127	113	110	127	128	108	95
Systemic blood flow (cc / min)	1780	2478	5420	5537	3835	4487	3500	4057	4264	4443	3686	2951
Pulmonary blood flow (cc /min)	1780	1318	5420	3987	3310	3325	3500	3343	3527	3208	3686	2039
% shunt	0	47	0	28	14	26	0	18	17	28	0	31

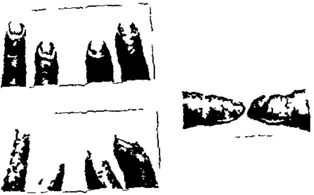


FIG 56—Unilateral clubbing on left is caused by a subclavian aneurysm On the right the unilateral clubbing is caused by multiple congenital arteriovenous aneurysms of the ipsilateral extremity (Mendlowitz[39] [illegible] courtesy Clinical Science)

endocrine disease is unconvincing and in the rare case in which it occurs probably fortuitous[401]

It is possible to present a theory that reconciles all the facts now known about the phenomenon of clubbing and hypertrophic osteoarthropathy The only justification for incurring the risk of subsequent modification is an attempt to point the way Such a theory must attempt to explain why clubbing occurs when it does and also why it does not occur under other circumstances

One may start from the known fact that in acquired symmetrical clubbing the digital arterial pressure is elevated and the digital flow increased after inhibition of sympathetic nerve discharge by indirect heating[389, 390, 42, 5] It can be calculated furthermore that the resistance in the digital blood vessels is either normal or decreased[405] It becomes apparent for this reason among others that the cause of the increased digital flow is largely the increased digital blood pressure and in general these two increases are proportional

It is necessary to inquire in turn as to what could cause an increase in digital arterial pressure without affecting the brachial blood pressure significantly[401, 6, b] One must conclude that a fine balance must exist between the demand of systemic tissues for blood and the supply[49] That this is so has been suggested by many authors[166, 170, 350, 482] although the exact mechanisms for adjusting supply to demand are not clearly understood The gradient of pressure from aorta to digital artery in the absence of obstructive arterial disease is not determined to any significant extent by the resistance of the vessels in a direct line but largely by the amount of pressure head tapped off by the tissues proximal to the digit[407] If there is an imbalance in the sense that the supply of blood is greater than the

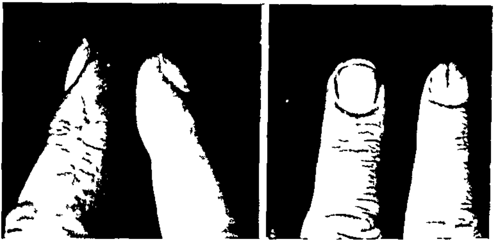


FIG 55A (left) and B (right) —This female typist develop d clubbing of the right finger after a laceration on the lateral asp ct just above the terminal interphalangeal joint This finger was warmer than the left in a cool environment but became slightly cooler than the left finger after inhibition of sym pathetic nerve discharge Because of pain she did not use this finger and developed superimposed disuse atrophy (Mendlowitz [401])

grade fever and presumably increased peripheral circulation [401] Anemia or methemoglobinemia may be severe without producing clubbing [46] Also, unilateral and unidigital clubbing as well as the clubbing of con genital heart disease are rarely associated with any change in sedimenta tion rate[401] and it is difficult to conceive of anoxemia as playing any role in unilateral or hereditary clubbed fingers In fact all the evidence is suggestive of tissue hyperoxia and hypernutrition as the most important and possibly the only factor in the genesis of clubbing [391 401 62 b]

There is also a recurrent view that endocrine disease is responsible at least for hypertrophic osteoarthropathy[58 176] and that clubbing and hypertrophic osteoarthropathy are therefore separate diseases All avail able evidence however, seems to favor the view that hypertrophic osteo arthropathy is merely an extension of the process of clubbing to more proximal tissues especially bones [391 401] and the evidence for associated

TABLE 25 —*The Digital Circulation in Three Cases After Blalock Taussig Operation for Tetralogy of Fallot (Mendlowitz and Touroff[401])*

		After indirect heating and TEAC (5 mg /kg)					
Patient	Age and sex	Artery used	Brachial B P	Digital B P		Digital blood flow (/cm m)	
				Right	Left	Right finger	Left finger
1*	31 F	Left subclavian	106/90 R A	74/44	48/38	0 244	0 274
2	16 M	Right subclavian	78/46 L A	28/?	62/36	0 142	0 257
3	8 F	Right subclavian		,0/?	80/?	0 284	0 359

The discrepancy in the results in case 1 was probably caused by vasospasm

systemic tissue demand, this favors the development of clubbing.[401] Thus if more blood per beat were ejected by the left ventricle than the capillaries of the systemic circulation were prepared to accept this would result in an increase in digital arterial pressure and flow by virtue of the fact that an excess of blood would perforce be delivered to the periphery.[401]

It is important to emphasize that increase in cardiac output alone does not necessarily produce clubbing since in such conditions as anemia,[249, 391] Graves disease,[389, 391, 6 b] fever,[62 b] etc.,[226] the cardiac output increase is in balance with the increased tissue demand for blood. In patent ductus arteriosus[148] and other left to right shunts, the increase in output flows through the shunt.[70, 401] If in Graves disease however a thyroidectomy is done and the tissue demand for blood decreases suddenly, the supply remaining increased, clubbing and even hypertrophic osteoarthropathy may develop.[121, 391, 401, 471]

The key to most kinds of symmetrical clubbing lies in the pulmonary circulation[229] and more specifically in the operation of the principle of equal output of both ventricles.[442] Any condition in which the pulmonary circulation is increased without a corresponding increase in the demand for blood in the systemic circulation promotes the development of clubbing.[401] Such an increase in pulmonary circulation may occur functionally, as in chronic mountain sickness,[420] because of inflammation, as in bronchiectasis,[391] tuberculosis,[391] or lung abscess,[391] or through a vascular tumor of the lung.[391, 68] Any condition[25] which produces a pulmonary arteriovenous shunt will have the same effect, such as arteriovenous aneurysms of the lung[464, 488] and intracardiac shunts, as in the tetralogy of Fallot.[391] Subacute bacterial endocarditis[117, 246, 380] probably acts by producing pulmonary inflammation because of bacteria and their local and circulating toxins.[391, 401] It is also possible that in ulcerative colitis,[506] regional ileitis[391] and sprue,[14] as well as in certain chronic liver diseases,[67] it is the effect of absorbed toxins on the pulmonary circulation which causes the clubbing.[401] In the case of the diarrheic[14, 73, 287, 401] and liver diseases[67] there is no concrete evidence that the action is via the pulmonary circuit and it is possible that the mechanism is similar to that in patients with Graves disease following thyroidectomy.[121, 401, 471] If there is an increase in pulmonary circulation produced by any of these mechanisms this must be followed by an increase in systemic circulation, and if the increase in the systemic circulation is out of balance with the demand of the systemic tissues for blood, the stage is set for the appearance of clubbing.[401]

With these thoughts in mind, it becomes comparatively simple to explain unilateral clubbing due to aneurysm as being again a case of oversupply of a given vascular bed because of decreased resistance of a dis

TABLE 26 —*The Digital Circulation in Contralateral Digits of Patients with Unilateral Clubbing (Data is Presented in Calories and Not Converted to Blood Flow)* (*Mendlowitz* [89])

Patient	Age and sex	Diagnosis	Before indirect heating				After indirect heating				Maximum heat elimination	
			Brachial B P		Digital B P		Brachial B P		Digital B P			
			Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
W B	50 M	Aortic insufficiency and right innominate aneurysm Clubbing of fingers of right hand	190/?	180/?	165/75 (4th finger)	150/70 (4th finger)	165/?	150/?	125/65 (4th finger)	125/65 (4th finger)	0 97 cal /cm²/min (4th finger)	1 16 cal /cm²/min (4th finger)
M M	60 F	Multiple congenital aneurysms of left arm Clubbing of all fingers of left hand except 5th finger					140/85	138/85	114/50 (4th finger) 122/50 (5th finger)	122/52 (4th finger) 122/52 (5th finger)	1 35 cal /cm²/min (4th finger)	1 49 cal /cm²/min (4th finger)
W C	48 M	Increased clubbing on the right because of Pancoast tumor of the lung at the right apex	115/85	110/85	92/75 (2nd finger)	92/80 (2nd finger)	105/80	105/82	85/75 (2nd finger)	85/75 (2nd finger)	*Note* Right hand grossly warmer than left before indirect heating and cooler after indirect heating This indicates involvement of sympathetic nerves on the right	
G A	59 M	Right subclavian aneurysm clubbing of the finger of the right hand	1[illegible]0/80	130/75							*Note* The right hand was always grossly warmer than the left	

8

HYPERTENSION, SYMPATHECTOMY, AND CORONARY OCCLUSION

THE effect of hypertension on the digital circulation can be shown to be produced by three major factors [8, 167, 407, 444] The first is an increase in sympathetic nerve discharge the second a change in the intrinsic vascular caliber produced by humoral or metabolic factors and the third is structural narrowing of terminal vascular channels [400] Since capillary pressure is normal in hypertension [141, 144] these changes involve chiefly the arterioles It should be stated from the start that unless the decrease in vascular caliber is extensive enough to increase the systemic resistance as a whole [167, 472] hypertension is not produced Local increase in resistance usually decreases local blood flow but has a minimal effect on blood pressure [401]

There are certain bizarre types of hypertension which do not fit into the categories described above and should be discussed separately The local digital hypertension and increase in blood flow in clubbing has already been discussed In coarctation of the aorta despite some disagreement [331, 413] the systemic resistance is increased by an obstruction in the main arterial conduit rather than in the arterioles [59, 244] After inhibition of sympathetic nerve discharge blood pressure and flow are increased in the fingers (table 27) [401] This can be nicely demonstrated by comparing the two extremities in cases where the coarctation is between the innominate and left subclavian artery [85] Although pulse propagation time and pulse pressure are decreased [244] mean blood pressure and flow beyond the coarctation after inhibition of sympathetic nerve discharge are usually normal [85, 401] In coarctation of the descending aorta mean pressure and flow in the great toe are usually normal after inhibition of sympathetic nerve

tended major vessel tapping off blood from the aorta[401] This can be demonstrated to occur in the early development of such conditions[389, 119, 6, 1] The later complications have already been discussed[391] The effect of sympathetic block by lesions also becomes clear inasmuch as it consists of increasing the overall blood supply to a part at least temporarily[391] Later, modifying factors may nullify this effect[414] The cause of hereditary clubbing however, continues to remain unknown[391] although the possibility of a local defect in sympathetic innervation has already been discussed[401] One may therefore tentatively conclude that all forms of clubbing may eventually be found to be caused by local oversupply of blood brought about by various mechanisms acting singly or in combination[401]

discharge [401] After operation the hemodynamic changes are often at least partially reversed [531 32] There are cases in which essential hypertension is associated with coarctation and these two factors must be separated in such cases and distinguished There may also be a rare case of abdominal aortic coarctation in which a renal factor causes a generalized increase in intrinsic resistance [148] Such cases may be amenable to autotransplantation of the kidney [331]

The common variety of essential hypertension begins by being neurogenic [39 401] That is to say in the early stage after inhibition of sympathetic nerve discharge by indirect heating supplemented by intravenous injection of a ganglion blocking drug brachial and *digital blood pressure and digital flow* and resistance all fall to within normal limits (table 8) Heightened neurogenic vasospasticity moreover persists as a rule throughout the clinical course of ordinary essential hypertension [11 391 39] even into the malignant phase [401] The brachial-digital pressure gradient however is normal in essential but decreased in malignant hypertension [445]

In addition neurogenic vasomotor tone is present in all *normal individuals* to a variable degree [372 392 412] and can be demonstrated to be a factor *in any type of hypertension* whether essential or not [392 497 441] *Essential neurogenic hypertension is such a common condition that it may fortuitously complicate* any other type of hypertension [401]

The greatest amount of controversy has raged around the humoral mechanism *of essential hypertension* [43 79 181b 192 48 607 529 623 686] That such a mechanism exists in human hypertension is not easy *to demonstrate* [401] Everyone *is agreed* that circulating norepinephrine may *increase* vascular *tone* by virtue of its sympathomimetic effect [4 156] *This is often seen in pheochromocytoma* [83 193] *and in* some cases paroxysmal hypertension may be follow*ed by fixed* hypertension [377] In paroxysmal hypertension the digital *pressure flow* and resistance after inhibition of sympathetic *nerve discharge* are often normal (table 28) [392 401] Whether other *circulating* substances can influence vascular reactivity in response to ordinary *neurogenic* stimuli is still questionable [471 446] *Many such substances* including the VEM VDM system [619] *angiotonin* [116] pherentasin [7] *hypertensin* [151b] renin [482] serotonin [449] cortisone [153b] and others have been implicated but convincing proof of the significance of these effects is still lacking [471 494]

As for intrinsic *or non neurogenic* vascular tone* itself this can be demonstrated to exist only *if it can* be reversed Such reversal can be *demon*strated in the digital circulation (table 28) *after* recovery from acute glo

*Whether such increase in intrinsic *caliber* is tonic or caused by intracellular *or extracellular* vascular edema is not yet clear

TABLE 27.—*The Digital Circulation After Heat and TEAC in the Upper Compared with the Lower Extremity of Patients with Coarctation of the Aorta* (Mendlowitz[401])

Patient	Age and sex	Diagnosis	Finger studies							Toe studies	
			Brachial blood pressure	Digital blood pressure	Blood flow (cc./cm./min.)	Vascular vol. index cm. of skin (cu. μ)	Vascular caliber (cm.)	Resistance (dyne sec./cm.)	Femoral blood pressure	Digital blood pressure	Blood flow (cc./cm./min.)
L.C.	33 F	Coarctation of the aorta Status post thyroidectomy	140/82	3LF 98/42	0.30	882	0.030	2 720 821		RGT	0.34
A.H.	13 M	Coarctation of the aorta	154/96	3LF 123/79	0.33	652	0.028	3 406 954		RGT 65/?	0.24
L.B.	15 F	Coarctation of the aorta Ovarian agenesis	138/88	3LF 136/80	0.45	828	0.030	2 685 342			LGT 0.11
G.P.	24 F	Atypical coarctation of descending aorta Associated essential hypertension	138/72	3LF 107/74	0.23	514	0.027	4 353 740			LGT 0.23
L.R.	32 F	Slight left ventricular hypertrophy Mitral insufficiency Coarctation of the aorta	116/74	3LF 94/55	0.34	924	0.031	2 401 429		LGT 74/?	0.24
J.M.	37 M	Adult type coarctation of the aorta	142/80	3LF 88/49	0.30	893	0.030	2 484 237	Left 116/96	LGT 91/?	0.22
J.B.	29 M	Coarctation of the aorta	154/98	128/70	0.40	904	0.030	3 548 910	Left 95/75	LGT 70/?	0.31

TABLE 28—*Continued*

Hypertensive							
				After body warming			
Patient	Age and sex	Diagnosis	Preliminary brachial B P (mm Hg)	Brachial blood pressure (mm Hg)	Digital blood pressure (mm Hg)	Digital blood flow (cc min)	Digital vascular resistance (units)
B B	20 F	Neurogenic hypertension	145/100	135/94	110/ 6	0 36	73
B R	27 M	Neurogenic hypertension	148/95	132/86	116/60	0 38	65
P R	24 M	Neurogenic hypertension	138/88	128/80	102/60	0 36	63
D S	18 M	Neurogenic hypertension	140/94	125/84	96/52	0 29	68
A D	23 M	Neurogenic hypertension	148/88	132/ 2	112/ 5	0 34	8
F C	40 F	Neurogenic hypertension	140/86	142/ 6	102/52	0 32	67
J J	27 M	Neurogenic hypertension	145/88	125/73	88/ 0	0 28	6
L L	24 M	Neurogenic hypertension	160/95	135/88	125/ 5	0 31	91
M M	17 F	*Pheochromocytoma*	157/120	145/70	120/80	0 38	8
L B	21 F	Acute glomerulonephritis	140/88	130/85	116/82	0 23	121
J N	38 M	Acute glomerulonephritis	180/118	158/102	155/84	0 21	163
		Recovered	134/80	134/84	110/82	0 30	90
E H	32 F	Acute glomerulonephritis	185/120	190/115	160/115	0 19	208
		Recovered	130/ 5	128/74	106/ 8	0 34	6
R M	21 M	Essential hypertension	155/ 0	155/70	103/ 3	0 23	110
H S	22 M	Essential hypertension	165/80	135/68	120/ 5	0 22	125
E K	34 M	Essential hypertension	175/120	1 /115	140/112	0 21	1 4
P L	20 M	Essential hypertension	180/ 05	155 95	120/92	0 29	103
G B	28 F	Essential hypertension	182/130	182 130	155 122	0 28	158
A C	35 M	*Essential hypertension*	60/104	62/102	128/100	0 28	116
L T	57 F	Essential hypertension	210/120	212/128	175/68	0 29	118
A F	58 F	Essential hypertension	175/96	1 8/90	120/94	0 26	111
A S	41 F	Essential hypertension	174/96	160/95	136/96	0 29	114
P S	4 F	Essential hypertension	235/125	212/134	160/115	0 28	141
E S	38 F	Essential hypertension	230 155	226/142	190/140	0 33	143
L L	25 M	Essential hypertension	165/108	6 /115	118/100	0 28	110
J S	24 M	Chronic glomerulonephritis	165/115	158/95	148/108	0 29	126
L N	35 F	Toxemia of pregnancy	85/108	195/102	182/94	36	110
I G	56 F	*Malignant hypertension*	250/ 30	238/125	226/130	0 23	218
J P	48 F	Malignant hypertension	255/135	240/134	212/112	0 26	180
D B	42 M	Malignant hypertension	220/150	215/155	198/154	0 16	319
I R	48 M	Malignant hypertension	238/ 50	245/135	205/112	0 17	2 0

Dig t l ascul es stanc i c lculated n units by di id ng arithmetic me n pre ure m nu e nou p essure by flow and m lt plying by 0 3

to decreased elasticity of the large arterial channels and is often associated with decreased diastolic pressure [610] Digital blood flow and resistance may be normal but associated arteriolar hypertension is common whether neurogenic of renal or intrinsic structural origin or any combination of these [39, 401, 404]

It is very likely that in certain conditions hypertension begins because of generalized structural narrowing of small blood vessels It is almost impossible to exclude the factor of associated renal hypertension[295] in such cases since the vessels of the kidney are often concomitantly in

merulonephritis[39] and after delivery in toxemia of pregnancy[39, 401] It is very likely, moreover, that part of the residual or intrinsic resistance[549] in more advanced essential hypertension is reversible and of renal or humoral origin It may be possible to demonstrate this by showing that the low sodium diet[130, 99, 300, 595, 599] has an effect on the intrinsic resistance rather than on blood flow and cardiac output[149] The mechanism of renal hypertension is still obscure, although the effect of the kidney on tissue water and electrolyte distribution has been implicated[6, 501]

Hypertension produced by adrenocorticotropic hormone,[4, 8] cortisone,[415] or desoxycorticosterone acetate[361] or in Cushing s disease[536] with resulting salt and water retention[123] is also probably humoral rather then neurogenic although we have had difficulty in demonstrating this in the digital circulation[401] There is some evidence that these hormones influence vascular reactivity[458a] to ordinary neurogenic stimuli as well as to circulating norepinephrine[473] Humoral hypertension in general, as already indicated, *may be and often is complicated by a neurogenic factor as well* as by structural vascular narrowing[39, 399, 401, 6, 3]

Increase in intrinsic resistance may be divided into two factors (1) functional or humoral as already discussed and (2) structural[400, 400] The latter *is that increase in intrinsic resistance which is not* due to reversible changes but which is caused by anatomic narrowing of the vascular bed[400] Such narrowing can be produced by intimal thickening thrombosis external constriction and encroachment of hypertrophied arteriolar muscle on the vascular lumen[400, 401] It can also be caused by obliteration of vascular channels especially capillaries in various ways[401] The systolic hypertension in generalized arteriosclerosis especially of the aorta is due

TABLE 28 —*The Digital Circulation in Normal Compared with Hypertensive Subjects (Mendlowitz[393])*

			Normal			
			After body warming			
Patient	Age and sex	Primary brachial blood pressure (mm Hg)	Brachial blood pressure (mm Hg)	Digital blood pressure (mm Hg)	Digital blood flow (cc/cm/min)	Digital vascular resistance (units)
P W	22 M	110/75	102/74	88/40	0 30	58
A S H	31 M	125/86	130/85	106/50	0 26	83
A R	25 M	118/88	112/82	84/70	0 34	63
W P	23 M	120/85	118/85	102/64	0 27	86
A F M	30 M	122/84	118/90	96/60	0 38	5
A L	24 M	118/75	108/74	104/64	0 34	69
A M	45 M	112/75	114/72	108/68	0 36	68
M M	31 M	125/84	115/86	98/55	0 34	63
A K	50 M	122/86	105/ 2	86/60	0 37	54
P S C	45 F	102/72	104/68	96/64	0 33	67
G J C	51 M	130/85	125/78	108 70	0 34	73
M C M	25 F	110/72	104/74	88/50	0 29	65

E R	34 F	34/ 07	6 47	Rt ymp thec my D5 L2, c mpl t pl h cctomy	5–50	o o R toe	6/ 3	o	o 9 Rt toe	70/ 20	256	o o Rt t e	94/ 40	33
		80/ 36	4 49	Left symp thectomy D6 L3 omplete pl nch tomy										
H S	54 F	80/ 56	4 48	R ght ymp thect my D5 L2 greate and le er pl ch n cectomy	9–50	o o Lt toe	266/ 34	97	o 19 Lt toe	170/ 5	270	o o Lt toe	40/ 30	10
		o/150	7–48	Left ymp the tomy D4 L2 gre ter and les e pla ch nicectomy										
J P	53 F	6/ 30	8 47	Right sympathectomy D4 L3 g eate pla chn cectomy	9–50	o 13 Lt toe	182/100	81	o 21 Lt toe	156/110	310	o 20 Lt toe	195/130	239
		88/112	9 47	Left sympathectomy D4 L3 gre ter splanch icectomy										
R R	50 F	230/11	5–4	Right ympathectomy D4 L3 greater pl nchnicectomy	9–50	o 20 Lt toe	210/110	244	o 21 Lt toe	160/90	331	o 21 Lt to	202/104	268
			6 47	Left ympathectomy D4 L3 gre ter planchnicectomy										
O P	38 M	95/130	4 46	Left ympathectomy D4 L2 greater planchnicectomy adrenal dener at on	11–50	o 11 Lt toe	148/98	1 6	o 13 Lt toe	145/95	214	o 14 Lt toe	150/95	224
		180/140	6–46	R ght sympathectomy D4 L2, greater planchnicectomy adrenal denervation										
A G	36 M	152/ 10	3–48	Right sympathectomy D2 L3 complete planchnicectomy Left sympathectomy D2 L2 greater splanchnicectomy	8–50	o 18 Lt toe	138/106	291	o 20 Lt toe	120/82	395	o 19 Lt toe	130/110	313

TABLE 29.—*The Digital Circulation After Sympathectomy for Essential Hypertension (Menlhouse and Touroff*[414]*)*

Name	Age and sex	Preop BP	Date of operation	Operation	Date of test	Pre TEAC and indirect heating: Digital bl flow (cc/cm³/min)	Pre TEAC and indirect heating: Brachial bl pres (mm Hg)	Pre TEAC and indirect heating: Vasc vol index (cu µ)	Post TEAC and indirect heating: Digital bl flow (cc/cm³/min)	Post TEAC and indirect heating: Brachial bl pres (mm Hg)	Post TEAC and indirect heating: Vasc vol index (cu µ)	Post benzodioxane: Digital bl flow (cc/cm³/min)	Post benzodioxane: Brachial bl pres (mm Hg)	Post benzodioxane: Vasc vol index (cu µ)
R S	51 F	210/120	10-46	Rt sympathectomy—D4 L2 greater splanchnicectomy partial celiac ganglionectomy adrenal denervation	11-50	0.21 Lt toe	166/86	328	0.24 Lt toe	120/82	474	0.22 Lt toe	160/95	338
		210/120	11-46	Left sympathectomy D4 L2 greater splanchnicectomy partial celiac ganglionectomy adrenal denervation										
S K	52 M	240/100	1-46	Rt sympathectomy D4 L2 greater splanchnicectomy partial celiac ganglionectomy adrenal denervation	1-51	0.06 Lt toe	174/90	89	0.11 Lt toe	190/100	148	0.11 Lt toe	185/100	151
		236/144	2-46	Left sympathectomy D4 L2 greater splanchnicectomy partial celiac ganglionectomy										
M B	55 M	260/150	3-48	Left sympathectomy D5 L3 complete splanchnicectomy	8-50	0.08 Lt toe	208/126	93	0.08 Lt toe	162/112	115	0.09 Lt toe	225/120	101
			4-48	Right sympathectomy D5 L3 complete splanchnicectomy										
J P	38 M	205/135	5-48	Right sympathectomy D3 L2 greater splanchnicectomy	8-50	0.05 Lt toe	148/106	78	0.09 Lt toe	140/110	142	0.12 Lt toe	160/100	182
		184/120	5-48	Left sympathectomy D4 L2 complete splanchnicectomy										

F R	38 F	215 39	1 45	R ght ymp h t my D4 L2 p c l l g ngl t my dr n l dener t n	3 5	0 04 Lt t	88/ 6	50	0 09 Lt t	40/ 5	38	0 10 Lt t	180/ 30	26
		160/ 05	9 45	Left ymp the t my D4 L2 complete planch icec tomy p tial c l g n gl o ect my dren l de e ati n										
R H	29 F	60/ 00	45	R ght ymp thect my D4 L2 compl te pl chnicec tomy parti l celiac g n gli ect my adr n l de ner ation	4 51	0 09 Lt toe	148/98	144	0 16 Lt toe	126/95	464	0 27 Lt toe	120/95	497
		1 0/ 04	8 45	Left ymp thectomy D4 L2, c mplete plan hnicec tomy parti l c l c gan glionectomy drenal de ner ation										
A C	52 F	218/134	7 46	Left ympathectomy D4 L2 complete splanchn cec tomy partial cel ac gan glio ectomy drenal de ner at on	2-51	0 12 Lt toe	222/130	232	0 13 Lt toe	1 2/112	179	0 14 Lt toe	254/154	133
		184/120	9 46	Right ympathectomy D4 L2, complete splanchn cec tomy partial celiac g n glionectomy adren l de ner ation										

TABLE 29 —*Continued*

Name	Age and sex	Preop B P	Date of operation	Operation	Date of test	Pre TEAC and indirect heating: Digital bl flow (cc/cm/min)	Pre TEAC and indirect heating: Brachial bl pres (mm Hg)	Pre TEAC and indirect heating: Vasc vol index (cu μ)	Post TEAC and indirect heating: Digital bl flow (cc/cm/min)	Post TEAC and indirect heating: Brachial bl pres (mm Hg)	Post TEAC and indirect heating: Vasc vol index (cu μ)	Post benzodioxane: Digital bl flow (cc/cm/min)	Post benzodioxane: Brachial bl pres (mm Hg)	Post benzodioxane: Vasc vol index (cu μ)
E S	45 M	250/172	1–48	Right sympathectomy D6 L1 complete splanchnicectomy	8–50	0.09 Lt toe	162/134	119	0.11 Lt toe	164/130	146	0.09 Lt toe	168/125	120
		160/100	6–48	*Left sympathectomy D6 L2*										
S T	47 F	250/120	7–46	Bilateral sympathectomy D4 L2 complete splanchnicectomy denervation of adrenal glands	12–50	0.21 Rt toe	196/98	279	0.23 Rt toe	160/94	357	0.22 Rt toe	190/108	299
M N	45 M	210/110	6–46	Bilateral sympathectomy D4 L2 celiac ganglionectomy greater splanchnicectomy adrenal gland denervation	12–50	0.06 Lt toe	228/138	64	0.17 Lt toe	230/130	183	0.16 Lt toe	208/136	181
J M	52 M	190/?	6–47	Right sympathectomy D4 L2 denervation right adrenal gland	8–50	0.06 Rt toe	142/96	100	0.05 Rt toe	110/70	112	0.05 Rt toe	144/88	85
		120/92	2 48	Left sympathectomy D4 L2 denervation left adrenal gland										
M D	26 F	220/140	6–48	Right sympathectomy D5 L3 greater splanchnicectomy	4–50	0.09 Rt toe	244/184	81	0.13 Rt toe	194/160	143	0.13 Rt toe	218/180	126
		240/160	9–48	Left sympathectomy D5 L3 greater splanchnicectomy										
R S	54 F	236/162	12–49	Left sympathectomy D8-L2 complete splanchnicectomy	5–50	0.21 Rt toe	1-6/126	272	0.18 Rt toe	138/108	289	0.17 Rt toe	136/104	280
			12–49	Right sympathectomy D9 L3 complete splanchnicectomy										

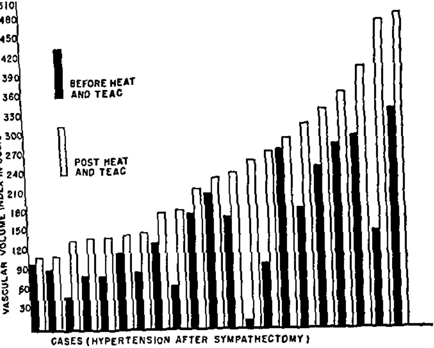
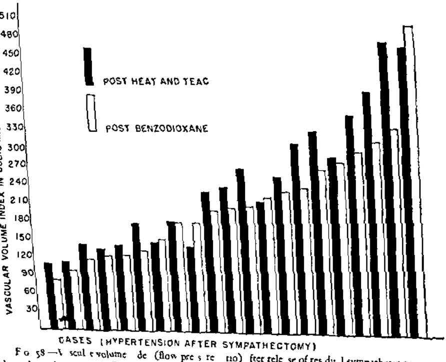


Fig 5 —Va cul r volume index (flow-pressure ratio) before and after release of re idual sympathetic nerve tone by indirect heating and TEAC (5 mg /Kg) Flo is measured calorimet ically in the great toe and pre s e s the a ithmetic brachial mean pre sure (Mendlov itz and Touroff [114] courtesy Grune & Str tton)



F o 58 —V scul r volume de (flow pre s re tio) fter rele se of res du l sympathetic nerve tone by i d ect h t ng and TEAC (5 mg /Y g) comp d with index after ben od ox e (10 mg per sq M) Flow i me red c lo imetr cally n gr at toe nd p es ure is the ithm tic brachial me n pre su e (Mendlowit a d To off co t y G un & Str tton)

TABLE 29—*Concluded*

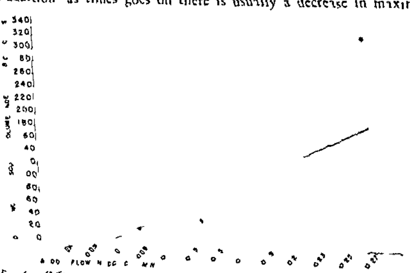
Name	Age and sex	Pre-op B P	Date of operation	Operation	Date of test	Pre TEAC and indirect heating			Post TEAC and indirect heating			Post benzodioxane		
						Digital bl flow (cc/cm²/min)	Brachial bl pres (mm Hg)	Vasc vol index (cu μ)	Digital bl flow (cc/cm²/min)	Brachial bl pres (mm Hg)	Vasc vol index (cu μ)	Digital bl flow (cc/cm²/min)	Brachial bl pres (mm Hg)	Vasc vol index (cu μ)
D R	41 F	184/104	10-46	Rt sympathectomy D4 L2 complete splanchnicectomy partial celiac ganglionectomy adrenal denervation	3-51	0.12 Lt toe	212/126	207	0.17 Lt toe	174/114	231	0.17 Lt toe	210/120	201
		168/92	11-46	Left sympathectomy D4 L2 complete splanchnicectomy partial celiac ganglionectomy adrenal denervation										
I S	37 M	270/130	4-45	Right sympathectomy D4 L2 complete splanchnicectomy partial celiac ganglionectomy adrenal denervation	1-51	0.12 Lt toe	162/114	171	0.14 Lt toe	132/100	239	0.14 Lt toe	155/110	207
		190/130	6-45	Left sympathectomy D4 L2 complete splanchnicectomy partial celiac ganglionectomy adrenal denervation										

trinsi or non neurogenic changes and include the humoral functional or reversible as well as the structural or relatively fixed factors

Therapy with drugs in hypertension is nearly always directed at the neurogenic factor [401] This neurogenic vasoconstriction is decreased very often by bed rest [157] sedatives [157] and blocking agents acting on the central nervous system [306] [611] sympathetic ganglia [331] [349] [306] or sympathetic nerve endings [331] [316] With 1 hydrazinophthalazine in ome cases we could demonstrate a decrease in intrinsic resistance as well as neurogenic resistance although the meaning of this is unclear [149] [401] The rice or low sodium diet when it decreases blood pressure, chiefly affects the intrinsic or non neurogenic components [149] Flow resistance, or both, may decrease with the pressure as demonstrated after inhibition of sympathetic nerve discharge [149]

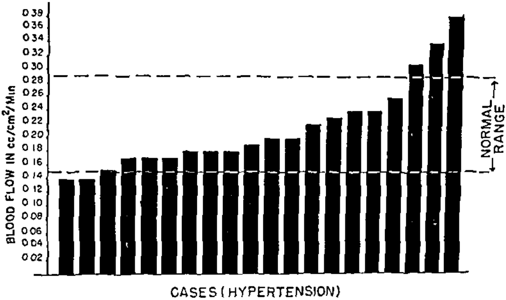
Thoracolumbar sympathectomy for hypertension produces an interesting train of vascular events (table 29) [31] [411] Immediately after the sympathectomy and for several days the interruption of sympathetic activity is usually complete Sympathetic nerve discharge, with resultant vasoconstriction then begins to return gradually [34] and eventually returns to a variable extent in every patient (fig 57) [411] This is due in part to bridging of nerve gaps by regrowth of fibers but also to the probable assumption of function by sympathetic ganglion cell nests known to exist in the anterior spinal nerve roots [*] [*] [*] [*] Also the sympathetic nerves in the upper extremities and those parts of the body not affected by the sympathectomy often develop excessive discharge with resultant compensatory vasoconstriction [321]

In addition as times goes on there is usually a decrease in maximal



F[illegible] Difference in [illegible] time index bel[illegible] and after [illegible] of symp thetic ner e tone el ted with bl ood fl w after rel ase of sympathetic nerve tone Correlat n ndc [illegible] (Mendlowitz [illegible] ute y C[illegible] ne & Stratt n)

volved [15] Diabetes mellitus,[304, 436, 5] lupus erythematosus[401] and pei arteritis nodosa[177, 319, 54] are conditions in which the structural factor often present from the beginning and may even initiate the hypertei sion [401] It cannot be overemphasized that in any type of hypertension, persistent for a sufficiently long period, there may be a large structur factor attributable to anatomic vascular changes which produce narrow ing [399, 401] Such changes, by their very nature, are reversible very slowly if at all and may properly be referred to as fixed or at least relativel fixed [39, 399] The resistance changes demonstrated in table 14[399] are in



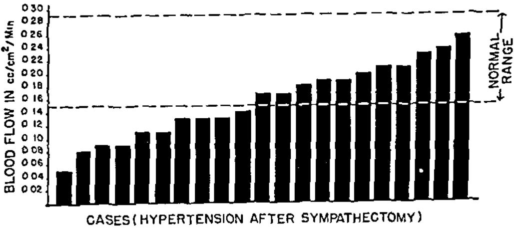


FIG 59A (top) —Blood flow in the great toe after release of sympathetic nerve tone by indirect heating and TEAC (5 mg /kg)

FIG 59B (bottom) —Blood flow after release of sympathetic nerve tone by indirect heating and TEAC (5 mg /kg) in the great toe (Both figures from Mendlowitz and Touroff [14] courtesy Grune & Stratton)

vascular caliber after sympathectomy [0, 221, 414, 415] which has been attributed by some authors[189, 199] to increased sensitivity to circulating epinephrine or norepinephrine (fig 58) The entire question of increased sensitivity to circulating epinephrine [601] however is complicated by the return of some sympathetic nerve function in all patients subjected to sympathectomy [414] There is unquestionable reactivity of denervated blood vessels to circulating epinephrine but whether these are more reactive than normal[152] has not been clearly established [393, 394] The question is further complicated by the demonstration that the decreased caliber of blood vessels after inhibition of residual sympathetic nerve discharge as produced by sympathectomy cannot be reversed by benzodioxane [414] and is probably not caused by epinephrine in the circulation (fig 59) [202] The fact that there is some correlation between the degree of success of the sympathectomy and the postsympathectomy decrease in maximal vascular caliber suggests shortening of arteriolar circular smooth muscle caused by disuse atrophy as possibly an important factor in this process (fig 60) [414] Despite these considerations there is good evidence that sympathectomy is of some value in selected cases of essential hypertension [188, 389, 28, 51, 612, 613]

After unilateral sympathectomy reflex vasodilatation may cause a relative decrease in flow on the denervated side because the blood is *re distributed* to other parts of the systemic circulation[184] (borrowing lend *ing effect*[478]) *It* is conceivable that this effect might produce paradoxic gangrene[157] after sympathectomy for occlusive vascular disease if there is already a severe impairment of *circulation*

Following coronary occlusion the digital blood flow after inhibition of sympathetic *nerve* discharge is usually decreased (table 30) [392] This decrease is due to a *proportionate* decrease in digital blood pressure the resistance remaining unchanged whether or not the patient had hyper tension prior to *his coronary* occlusion [392] The decreased blood flow is hence a direct result of the decreased contractile force of the heart which is out of balance with the resistance and hence produces decreased arterial pressure and flow [228, 230, 446, 311]

Patient	Age and	Clinical course	Electrocardiogram	Date of onset of symptoms	Date of observations	Previous brachial blood pressure (mm Hg)	Preliminary brachial blood pressure (mm Hg)	After body warming: Brachial blood pressure (mm Hg)	Digital blood pressure (mm Hg)	Digital blood flow (cc/cm²/min)	Digital vascular resistance (units)
B S	55 M	Typical second attack	Progressive change	5-19-41	6-6-41	230/?	142/90	130/86	130/85	0.15	204
B M	63 M	Typical	Progressive change	5-13-41	6-20-41	Unknown	120/88	112/85	88/72	0.24	92
S P	52 F	Typical	Progressive change	7-2-41	8-4-41	High	126/80	126/90	118/102	0.30	104
E S	48 F	Typical	Progressive change	7-25-41	8-23-41	200/?	160/102	164/102	140/78	0.20	154
A O	52 M	Typical	Progressive change	8-19-41	9-19-41	140/96	118/84	116/76	110/76	0.16	163
S W	59 M	Typical	Progressive change	9-2-41	9-30-41	Unknown	135/95	108/82	98/68	0.13	177
J K	47 M	Typical	Progressive change	9-8-41	10-8-41	132/92	116/72	110/74	102/64	0.18	127
A B	60 F	Typical	Progressive change	9-30-41	10-25-41	Unknown	105/85	88/68	72/60	0.22	82
H M	63 M	Typical	Progressive change	11-22-41	12-6-41	Unknown	116/78	118/76	100/64	0.20	114
N A	62 M	Typical second attack	Progressive change	10-12-41	11-16-41	Normal	100/72	98/74	70/48	0.18	89
B L	55 F	Typical second attack	Equivocal	7-9-41	7-23-41	190/?	138/100	138/94	125/86	0.19	158
M N	50 F	Typical	Equivocal	8-9-41	9-18-41	160/110	125/88	128/88	104/90	0.20	136
A G	67 M	Typical	Equivocal	8-27-41	10-2-41	Unknown	120/90	98/76	96/60	0.24	90
S D	63 M	Typical	Equivocal	10-24-41	11-17-41	150/90	135/65	124/68	106/64	0.18	113
P N	43 M	Typical	Equivocal	11-8-41	11-7-41	Unknown	135/90	116/74	98/70	0.13	166
R S	58 F	Atypical	Progressive change	5-9-41	6-10-41	180/?	160/80	150/85	118/92	0.31	96
G L	58 F	Atypical	Progressive change	7-9-41	8-1-41	180/?	165/75	145/72	102/70	0.29	92
M H	40 F	Atypical	Progressive change	11-17-41	11-29-41	High	150/92	138/76	108/74	0.23	111
M M	65 F	Atypical	Progressive change	11-27-41	12-10-41	High	155/68	142/50	96/72	0.16	146
S B	52 F	Atypical	Progressive change	12-4-41	12-20-41	190/85	158/88	148/78	124/86	0.18	165
S V	63 M	Atypical second attack	Equivocal	10-2-41	10-31-41	180/100	150/84	150/85	114/72	0.26	101
J G	50 M	Atypical second attack	Equivocal	10-31-41?	11-11-41	Unknown	110/68	110/80	98/56	0.32	67
D R	39 M	Atypical	Equivocal	10-1-41?	11-3-41	150/?	130/88	142/94	118/84	0.20	142
S K	48 M	Typical	Progressive change	7-5-40	11-24-41	Normal	125/88	116/84	92/78	0.38	62
S S	64 M	Typical	Progressive change	5-6-36	11-14-41	140/90	155/95	138/90	115/80	0.27	102
B M	55 M	Atypical	Progressive change	2-19-41	11-16-41	150/110	142/98	138/84	120/82	0.29	204

TABLE 31.—The Digital Circulation in Anemia and Polycythemia (The Resistances Are Calculated as in Table 28) (Maloney[335])

Name	Age and sex	Diagnosis and therapy	Date	Hematocrit	Digital blood flow (cc/min/100 cc)	Digital arterial blood pressure (mm Hg)	Intravenous pressure (mm Hg)	Digital resistance (units)	Rate of abnormal viscosity*	
[illegible] S	3 F	Aplastic anemia treated by transfusions	4 14 42	17	0 36	88/60	10	52	80	1/1 25
			4 15 42	19	0 36	86/65	10	54	82	1/1 22
			4 18 42	22	0 36	98/68	11	60	91	1/1 10
			4 24 42	22	0 32	90/62	11	61	9[illegible]	1/1 09
			4 2[illegible] 42	26	0 32	94/68	11	65	98	1/1 02
			4 30 42	31	0 30	86/60	12	61	92	1/1 09
			5 6 42	35	0 31	9[illegible]/62	13	62	94	1/1 06
			5 8 42	38	0 30	9[illegible]/58	13	62	94	1/1 06
			5 11 42	42	0 29	92/64	14	66	1 00	1/1 00
[illegible] M	54 M	Pernicious anemia treated with folic acid	1 9 47	21	0 28	94/56	11	69	81	1/1 23
			[illegible] 14 47	25	0 26	94/48	11	[illegible]	93	1/1 21
			1 21 47	30	0 29	104/58	12	[illegible]	85	1/1 18
			1 28 47	34	0 2[illegible]	106/64	13	80	95	1/1 05
			[illegible] 4 [illegible]	36	0 28	116/65	13	82	98	1/1 02
			3 15 47	38	0 31	120/80	14	83	99	1/1 01
			5 28 4	42	0 32	122/84	14	84	1 00	1/1 00

* The ratios are rearranged in this column to correspond with the graph of Whittaker and Winton[433] in order that the points observed in figure 1 may be compared with the curve obtained by these authors

Thus anemia decreases the viscosity to a greater extent and may increase the Reynolds number[452] to a point where turbulence begins,* thus producing the hemic murmur so common in extreme anemia.[410] Pressure and velocity changes are additional factors.[410] In polycythemia, on the other hand, viscosity may be increased to a point where organic murmurs can no longer be heard.[311] Table 31 shows circulatory changes in the digital circulation with anemia and polycythemia after inhibition of sympathetic nerve discharge.[396, 399] This is represented graphically in figure 43. These effects are often obscured by superimposed reflex responses.[333]

The findings in polycythemia demonstrate that the increased resistance produces some increase in blood pressure but chiefly a decrease in flow. However, since each cubic centimeter of arterial blood contains a larger absolute quantity of oxyhemoglobin this would not cause anoxemia until a critical point were approached.[401]

In anemia the effect on viscosity is definite but not very great. It must be remembered, however, that this is true of arteriovenous anastomotic

* The Reynolds number is calculated from the formula $\frac{VDP}{\eta}$ where V is velocity, D tube diameter, P pressure and η viscosity. Turbulence usually begins at 1000 units for plasma and 2500 units for cells.[1]

9

ANEMIA AND POLYCYTHEMIA

CHANGES in intravascular blood viscosity with anemia and polycythemia have already been discussed (p 82) in part The in vitro changes in viscosity with varying erythrocyte concentration are not in accord with what happens in vivo, or more specifically in the digital circulation [394, 395] It has been estimated from in vitro studies, for example, that in extreme polycythemia blood viscosity may increase from 5 to 11 fold [6, 7, 634] Since, from Poiseuille's law if pressure remains unchanged, this implies an 80 to 91 per cent decrease in blood flow or cardiac output, there must be an error involved This error is caused by the difference in the caliber of the tubes through which blood which is a two phase colloidal system flows The greatest frictional stress is always nearest the outer margin of the stream If the cells become crowded together[140] at certain critical tube diameters the proportion of plasma rim increases In general the larger the tube the smaller the area of rim in proportion to the entire cross sectional area This phenomenon (Fahraeus[151]) causes a decrease in intravascular blood viscosity as compared with that measured in vitro In anemia on the other hand the viscosity decreases more in vitro than it does in vivo for any given hematocrit At a hematocrit of 70 to 80 which is about the highest seen during life the intravascular viscosity of the blood rises to about double the normal [395, 399] If everything else remains unchanged this is capable of reducing flow to half the normal Anemia on the other hand even if extreme, decreases the intravascular viscosity to only 80 per cent of normal and is hence capable, on the basis of viscosity changes alone of increasing flow only to 120 per cent of the normal volume [396] This applies only to streaming flow in the small blood vessels In the large vessels and in the

10

MISCELLANEOUS CONDITIONS

THERE are many conditions in which the digital circulation has been investigated in only a fragmentary way or not at all In Addison s disease [361, 536, 537] for example as well as in traumatic shock it is difficult to obtain untreated cases or to delay treatment sufficiently so that investigation may be made In a few cases of Addison s disease as well as traumatic shock which were studied however we found blood pressure and flow decreased and resistance unchanged after inhibition of sympathetic nerve discharge [473] Flow is also decreased reflexly [165, 395] in shock and changes in viscosity with increased erythrocytic concentration may complicate the findings further [511] We have also studied flow and pressure in the digital circulation in a pressure chamber at a simulated altitude of 30 000 feet [401] Sympathetic nerve discharge was inhibited by heat and oxygen was administered by special mask No significant changes in the digital circulation were found which could be attributed to the formation of nitrogen bubbles in the blood The only vascular neoplasm that is common in the digit is the glomus tumor [378] This has been studied pathologically for the most part (p 30) rather than physiologically It is an extremely painful lesion curable by excision [17]

In Graves disease sympathetic vasomotor tone was decreased as measured by flow pressure ratio differences before and after inhibition of sympathetic nerve discharge After such inhibition however pressure flow and resistance were normal [401, 622b] *Apparently the effect of hyperthyroidism on* capillary circulation is too small to be reflected measurably in the total digital circulation which is largely *through* arteriovenous anastomoses Flow pressure and resistance were also usually normal after inhibition of sympathetic nerve discharge *in various* chronic infections with or without

TABLE 31 —*Continued*

Name	Age and sex	Diagnosis and therapy	Date	Hematocrit	Digital blood flow (Gm / cm min)	Digital arterial blood pressure (mm Hg)	Intercept (mm Hg)	Digital vascular resistance (units)	Ratio of abnormal to normal viscosity
A M	54 M	Primary polycythemia treated by repeated phlebotomy	3-29-47	61	0 20	85/50	19	74	1 35
			4-11-47	59	0 22	84/52	19	67	1 22
			4- 4-47	56	0 22	74/50	18	60	1 09
			4-16-47	54	0 24	82/54	17	64	1 16
			4-23-47	53	0 21	75/48	17	63	1 15
			4-28-47	50	0 22	72/48	16	60	1 09
			4/30/47	47	0 23	76/50	15	62	1 13
			5/ 5/47	42	0 25	70/50	14	55	1 00
L L	52 M	Primary polycythemia treated by repeated phlebotomy	3-14-47	61	0 20	88/72	19	92	1 39
			3-17-47	62	0 19	94/60	19	92	1 39
			3-24-47	51	0 21	81/55	17	73	1 11
			4-18-47	43	0 24	80/54	14	66	1 00
J L	60 M	Primary polycythemia treated by repeated phlebotomy	9-17-41	65	0 14	88/66	20	122	1 36
			10- 6-41	49	0 19	94/64	15	101	1 12
			10-15-41	42	0 21	90/64	14	90	1 00
L C	36 M	Primary polycythemia treated by repeated phlebotomy	7- 2-42	73	0 19	120/100	23	137	1 69
			7- 6-42	66	0 23	120/76	20	102	1 26
			7-10-42	59	0 24	118/94	19	109	1 34
			7-21-42	53	0 21	100/74	17	100	1 24
			7-25-42	47	0 23	104/78	15	98	1 21
			7-30-42	45	0 27	112/84	14	93	1 15
			8- 4-42	43	0 28	106/74	14	81	1 00

circulation chiefly [396] It is not known what takes place in the capillaries although correspondence between the experiments of Whittaker and Winton[600] and those on the digital circulation suggest that when the vessels of the dog s leg are fully dilated the relationship between blood flow and pressure through this largely capillary bed is nearly rectilinear It would be of interest to know the effect of hypoproteinemia on viscosity in vivo Whittaker and Winton[600] have made a beginning in this direction and Coulter and Pappenheimer[118] have suggested that the effect might be greater than expected in vitro because the plasma again occupies the position in the perfused vessel where the greatest frictional stresses occur namely the outer rim Definite data on the effect of hypoproteinemia on the digital circulation however, are not available

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fever (table 24)[390] These statements are all based on few observations and merely indicate observed trends rather than statistically valid conclusions

In disseminated lupus erythematosus in the acute phase,[30, 369, 533] no change in resistance or pressure in the digital vessels could be demonstrated *unless the disease were associated with Raynaud s phenomenon or sclerodermatous changes*[306, 307, 401] In the early phases of the disease the resistance was normal even in the presence of vascular lesions in the finger tips[401] This suggests that the arteriovenous anastomoses remain unaffected, the vascular lesions being by inference confined to the capillaries In periarteritis nodosa it is also difficult to demonstrate abnormality in the digital circulation unless there are local lesions producing Raynaud s phenomenon or hypertension due to renal disease[401] The associated fever makes the interpretation of tests difficult

Study of the digital circulation by the various methods which have been developed has been of value in elucidating a number of hitherto obscure problems of physiologic and clinical interest and gives promise of further expansion of our knowledge in many related areas There is need, for example for a competent study of the digital circulation in congestive heart failure despite reluctance to administer ganglion blocking drugs to such patients Many other avenues of investigation remain unexplored in this field and open to the curious scientists of the future

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